TO STUDY THE INCIDENCE OF CLUSTER SEIZURES AND EVALUATION OF PHARMACOLOGICAL MANAGEMENT STRATEGIES AMONG COHORT OF PATIENTS WITH EPILEPSY

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Submitted By

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I hereby declare that the thesis entitled **"TO STUDY THE INCIDENCE OF CLUSTER SEIZURES AND EVALUATION OF PHARMACOLOGICAL MANAGEMENT STRATEGIES AMONG COHORT OF PATIENTS WITH EPILEPSY"** submitted towards partial fulfillment of the requirements for the award of **MD IN PHARMACOLOGY** degree to BFUHS is a compilation of original work carried out by me under the supervision of **Dr. Sandeep Kaushal**, Professor & Head, Department of Pharmacology, **Dr. Gagandeep Singh**, Professor & Head, Department of Neurology & **Dr. Kanchan Gupta**, Professor, Department of Pharmacology. No part of this thesis has formed the basis for the award of any degree previously.

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Dedicated

to

my Family

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Dr. Simrat Kaur

LIST OF ABBREVIATIONS

ADR: adverse drug reaction

ARS: Acute repetitive seizures

ASM: antiseizure medications

CBZ: carbamazepine

E: excitation

FBM: felbamate

FDA: food and drug administration

GTCS: generalized tonic clonic seizures

I: inhibition

ILAE: International league against Epilepsy

LTG: lamotrigine

MTS: mesial temporal sclerosis

OXC: oxcarbazepine

PHT: phenytoin

PWE: patients with epilepsy

RSE: Refractory Status Epilepticus

SC: seizure clusters

SE: status epilepticus

SUDEP: sudden unexpected death in the epilepsy

TPM: topiramate

WHO: World health organization

ZNS: zonisamide

ABSTRACT

Introduction: Many people with epilepsy (PWE) report seizures that occurs in close successions; which are termed as seizure clusters (SC), acute repetitive seizures (ARS), or crescendo seizures. The primary treatment of seizure clusters is Antiseizure medications (ASMs). These repetitive seizures are not very uncommon and place a burden on patients and their caregivers. Thus, this study was planned to look for the incidence of cluster seizures and their pharmacological outcome among cohort of patients with epilepsy.

Objectives: To study the incidence of cluster seizures among cohort of patients with epilepsy and evaluation of pharmacological management strategies in patients with epilepsy.

Methods: This observational study was conducted in 184 patients with epilepsy on antiseizure medications (ASMs) among people attending neurology OPD and epilepsy clinic at Dayanand Medical College, Ludhiana. Demographic data and drug history was collected. Follow up period was 3 months. Data regarding seizures frequency, type of epilepsy, dose of ASMs were recorded in a semi structured proforma. Number of seizures in a day were recorded. Results were correlated with patient demographics, dose, type, frequency and number of ASMs.

Results: Out of 184 patients, 73 patients had clustered seizures. Out of them, 7 patients were lost to follow up. Data of 66 patients was analyzed. 37 patients had controlled seizure clusters at the end of follow up period. Among those 4 patients were on monotherapy and 33 patients were on polytherapy.

Conclusion: Incidence reported was 39.6% among cohort of people with epilepsy. Stress was the most common risk factor for the development of cluster seizures. Drowsiness was the most common ADR in patients who were on commonly prescribed ASMs such as levetiracetam, clobazam, carbamazepine, sodium valproate and oxcarbazepine.

Keywords: cluster seizures, epilepsy, incidence.

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INTRODUCTION

The World Health Organization (WHO) has recognized epilepsy as a major public health concern. According to the WHO, about fifty million people worldwide are affected by epilepsy, which makes one of the most common neurological diseases worldwide[1]. Although numerous underlying illness mechanisms can contribute to the epilepsy, the origin of the condition is unknown in approximately half of all global cases[2]. Epilepsy is a disorder characterized by abnormal neuronal discharges or hyperexcitability of neurons with synchrony without provocation, resulting in seizures. The condition is classified into three subgroups: acquired, idiopathic, and epilepsy with genetic or developmental origins[1]. The imbalance between excitation and inhibition, leads to seizures[3]. A "seizure" is a paroxysmal change in neurologic function induced by an abnormal, hypersynchronous discharge of brain neurons. The term "epileptic seizure" distinguishes between a seizure induced by aberrant neuronal firing and a nonepileptic event, known as psychogenic seizure. Epileptic seizures are jerky or quivering movements in the body caused by aberrant neuronal activity, which can cause harm to the brain or other organs. Even single seizure can produce abnormalities in brain development, resulting in behavioural and cognitive problems[4]

The International League against Epilepsy classified seizures into major types namely generalized seizures which involve both hemispheres of brain and partial (focal) seizures which begin locally in one part of brain[5].

Diagnosing epileptic seizures and epilepsy, and determining the aetiology, are tough undertakings, especially in lowincomecountries where socioeconomic and cultural barriers prevent the disease from being accepted[6]. The most common clinical signs are recurring muscular twitches, and shortterm disturbances in sensation and consciousness. In severe cases, it may develop symptoms like loss of consciousness and generalized tonic clonus[7]

It’s a burdensome neurological disease known to increase mortality by 10 folds among affected population[8]. About 1% of population suffers from epilepsy, and about one third of the patients suffer from refractory epilepsy (i.e., seizures which are controlled by two or more than two appropriately chosen antiseizure medications or other therapies). Approximately 75% of epilepsy cases begin in childhood, indicating that developing brain is more susceptible to seizures[4].

Epilepsy is associated with a variety of risks, including sudden unexpected death in the epilepsy (SUDEP), status epilepticus, drowning, pneumonia, motor vehicle and bicycle accidents, falls, burns, and suicide. Drugs which are used to treat epilepsy can also cause rare, fatal allergic reactions and increase risk of obesity and cardiovascular disease[9].

Several factors influence burden of disease, including seizure type and the response to antiseizure medications (Strzel czyk et al., 2008). According to the Global Burden of Epilepsy study 2019(GBD2019), idiopathic epilepsy and epilepsy due to other causes, altogether, resulted in 18.3 million (95% UI 12.3−24.8) global years lost due to disability (YLDs) in 2019 and were responsible for 2.1% (1.6−2.7) of total global YLDs[10]

Many people with epilepsy (PWE) report seizures that occurs in close successions; which are termed as seizure clusters (SC), Acute repetitive seizures (ARS), or crescendo seizures[11]. The frequency of the cluster seizures has been reported in the range of 3% - 76% worldwide among people with epilepsy[12]. Prevalence of the cluster seizures varies significantly in the different studies depending upon the definitions used in that particular study. In a study by Haut Et al Forty three percent of patients who maintained a seizure diary met the clinical criterion of having three or more seizures in 24 hours[13].

A similar phenomenon to cluster seizures called the “rebound effect” is characterized by an increased in occurrence of epileptic seizures following an abrupt withdrawal of antiseizure medications (ASMs)[14].

Refractory Status Epilepticus (RSE) is typically the result of an acute neurologic illness or a neurodegenerative disease. RSE is difficult to treat, requiring intensive support of essential functions [15].

Extra doses of antiseizure medicines are commonly used to treat minor seizure clusters. In addition, benzodiazepines diazepam, and lorazepam can be used (oral clobazam or sublingual benzodiazepines) in particular diazepam, and lorazepam[16]. These repetitive seizures are not very uncommon and place a burden on patients and their caregivers. These closely related seizures imply a serious clinical condition, and if not treated vigorously and effectively, may lead to a condition called status epilepticus (SE), a life-threatening condition[17]. History of patients with seizure clusters and status epilepticus , head trauma , earlier age of onset of seizure and high seizure frequency in one year after the onset of epilepsy (one weekly seizure or more) are associated more with seizure clusters.[18]

We have planned this study to evaluate incidence of seizure clusters in our cohort of population and look at effectiveness and sequelae of various pharmacological treatment modalities employed longitudinally over period of time. The study includes retrospective follow up of 3 years and prospective follow up of 1 year in clusters.

AIMS & OBJECTIVES

1. To study the incidence of cluster seizures among cohort of patients with epilepsy
2. Evaluation of pharmacological management strategies in patients with epilepsy

REVIEW OF LITERATURE

A seizure can be defined as an occurring when there is disturbance in the normal balance between excitation (E) and inhibition (I) in the brain. This imbalance in E/I can be caused by changes at various degrees of brain function, including genes, subcellular signalling cascades, and broad neural circuits. A change in the E/I balance can be a result of number of sources, including acquired or inherited. Epileptic genetic disorders can originate at any level, from the receptor to the circuit level (e.g., aberrant synaptic connection in cortical dysplasia)[19]. Epilepsy, an illness characterized by unprovoked seizures, is a complicated disease with various causes that affects people of all age groups, with special emphasis on the very young population and the elderly. In addition, many patients also experience cognitive and psychological difficulties that are related with both the seizures and their therapy [20]

Epileptogenesis is a biological process that results in the occurrence of the first recurring epileptiform episode and spontaneous seizures. Epileptogenesis involves two GABA receptors, GABAA and GABAB. It is one of the main inhibitory neurotransmitters. Epileptogenesis occurs in three different phases, the first being an initial trigger (such as stroke, infections, and traumatic brain injury), followed by the latency period and the emergence of spontaneous and repetitive seizures that characterize epilepsy[21]. The primary mechanisms involved are inflammation, neurogenesis, neuronal migration to different regions of the brain, and neural reconfiguration. Presynaptic potentials are generated by hyperpolarizing neurons, which is critical for counterbalancing neuronal excitation and inhibiting epileptic discharges[22]

Seizure classification is a crucial factor in establishing the treatment strategy, because antiepileptic medicines have distinct actions against various seizure types. The International league against Epilepsy (ILAE) has classified epilepsy as [23]

(A) Focal seizures

1. Motor

-Tonic

-Atonic

-Myoclonic

-Epileptic spasms

-Clonic

-Hyper motor

2. Non motor

-Sensory

-Emotional

-Autonomic

-Cognitive

(B) Generalized

1. Motor

-Tonic clonic

-Myoclonic

-Tonic

-Atonic

- Clonic

-Epileptic spasms

2. Absence

-Typical

-Atypical

-Myoclonic

(C) Unknown onset

1. Motor

-Tonic clonic

-Atonic

-Epileptic spasms

2. Non motor

(D) unclassified

Seizure cluster is not enlisted in the International League Against Epilepsy (ILAE) Commission on Classification and Terminology. There is no universally agreed definition of a cluster of seizures among people with epilepsy. Seizure clusters are broadly defined as abrupt bouts of worsening in seizure control. Clinically, it is roughly characterized as two or more than two seizures in six hours, two or more seizures in 24 hours, two to four seizures in less than 48 hours, and two generalized tonic-clonic seizures (GTCS) or three complex partial seizures in four hours. It could also be described as a sequence of grouped seizures with short interictal durations[24]. Seizures that happen within eight hours are thought to be likely to originate from a consistent focus and are not truly "independent." [25]. According to one study, ipsilateral hemispheres were more likely to be the source of seizures with shorter interictal periods than those with longer intervals[26]. According to Saba et al., a cluster seizure is "an episode of multiple complex partial or generalized (tonic, clonic, tonic clonic, atypical absence, or myoclonic) seizures occurring within a 24-hour period in adults or a 12-hour period in children, with a pattern which is distinguishable from the patient's usual seizure pattern, and with onset readily recognizable by patients or guardians"[27]. These are also known as acute repeated seizures. According to surveys of patients and their guardians, seizure clusters have a detrimental influence on

the quality of life, emotional health, everyday function, and productivity of patients and their caregivers, which is accountable for the burdensome neurological illness[28]. However, medical treatment of epilepsy with first line antiseizure medications can render up to 70% of patients seizure free when seizures are adequately treated[29]. There is no commonly accepted definition of "seizure cluster," either in clinical trials or in clinical practice. As a result, the prevalence reported of seizure clusters among people with epilepsy ranges from 13% to 76%, indicating that this is not a minor health issue[30]

Although there are several treatments available to manage recurrent seizures, such as drugs, diets, immunomodulators, surgery, and neuromodulatory devices, many patients suffer the effects of uncontrolled seizures continuously. Individuals who have an age dependent epilepsy syndrome but are now over the appropriate age, or those who have been seizure free for the last 10 years with no seizure medications for the last 5 years, are regarded to have resolved epilepsy. In accordance to the new definition, epilepsy is now labelled as a disease rather than a disorder, comparable to other heterogeneous disorders like cancer and cardiovascular disease, which are also termed as illnesses to express the severity of the disease[20].

Individual seizures are usually self-limiting due to coordinated activities at several brain levels (circuit, cellular, and molecular). Seizure clusters alter GABAergic processes and cause synaptic potentiation, increasing the risk of future seizures[29,30]

Prevalence of seizure clusters significantly varies in different studies depending on the various definitions used[25]. Forty three percent of the patients who were maintaining a seizure diary met the clinical definition of having 3 or more than 3 seizures in 24 h, whereas only 22% of population have met the statistical definition[18]. Prevalence also depends on the research population. Most research on cluster seizures have been undertaken in tertiary epilepsy centres, where cases of refractory epilepsy are more common[31]. As a result, the prevalence

reported may be an overestimation. The prevalence of seizure clusters varies between 13 to 76% in the outpatient situation, and 18 to 83% in the inpatient setting[32]. In a study of adult outpatients, the prevalence of seizure clusters (3 or more seizures in 24 hours or three times the baseline frequency) was 14.9%[31]. Another study which involved both inpatient and outpatient settings found a 29% prevalence of three or more seizures in 24 hours[33].The prevalence in the inpatient setting has been reported to be 50 percent or higher. In addition to the selection bias and more severe epilepsy patients in the inpatient environment, in long-term monitoring units, anti-seizure drugs are sometimes temporarily withdrawn, which might trigger seizure clusters[25].

Some studies have been suggested that patients of extratemporal epilepsy [33], especially patients with frontal lobe epilepsy are more likely to have seizure clusters. Mesial temporal sclerosis (MTS) has also been linked to seizure clusters [34]. Seizure clusters are also linked with a history of CNS illness and localized cortical dysplasia. Seizure clusters are connected with a history of seizures and status epilepticus, head trauma, an early age of initiation of seizure, and a high frequency of seizures in the first 12 months following epilepsy onset (one weekly episode or more) [28]. The most important risk factor for seizure clusters is intractable epilepsy with a high frequency of seizures[35]. Also, it can be saif that clustering of seizures may indicate poorly controlled epilepsy [33]. The more the seizure frequency each day, the more probable they will meet the clinical criteria of clusters (more than three seizures in 24 hours) [25]. Several risk factors have been identified, including sleep or sleep deprivation, stress, fever or illness, missing or change in medications, alcohol and menstruation [36].

Unlike other therapeutic classes, anti-seizure medicines are rarely classified based on their modes of action. First, their molecular actions are not fully understood, and current knowledge indicates that most antiepileptic drugs have multiple mechanisms of action, each of which contributes to therapeutic efficacy to varying degrees depending on the

condition being treated [37]. Second, due to our limited understanding of how medications interact with disease pathophysiology, the strategy to treating epilepsy, as well as most other disorders in which AEDs are utilized, is not mechanism-based [38]. Blockade of voltage-dependent sodium channels is a primary action of phenytoin (PHT), carbamazepine (CBZ), oxcarbazepine (OXC), lamotrigine (LTG), topiramate (TPM), zonisamide (ZNS), and felbamate (FBM) [37]. Drugs which are used to treat epilepsy work by decreasing brain electrical activity, either by preventing neuronal depolarization by blocking sodium or calcium channels, improving potassium channel function, inhibiting excitation caused by the neurotransmitter glutamate, or by inhibition via GABA. The efficacy of these antiseizure medications (ASMs) differs according to their aetiology as well as semiologies. Patients who meet normal developmental milestones are mostly cured if there is no obvious cause[4]. Levetiracetam has gained popularity as a first-line treatment in recent years because of its high efficacy, ease of titration, and well-documented adverse reaction profile. Previously it was well known that carbamazepine was the first option for focal seizures, whereas valproic acid was the first choice for patients with generalized seizures.

According to Biopharmaceutics Classification System of antiepileptic medications, antiepileptic drugs can be classified into: [39]

Older drugs (FDA approved before 1993)

- Carbamazepine
- Clonazepam
- Ethosuximide
- Phenobarbital
- Phenytoin
- Primidone
- Valproic acid

Newer antiepileptic drugs

- Felbamate
- Gabapentin
- Lamotrigine
- Levetiracetam
- Oxcarbazepine
- Pregabalin
- Tiagabine
- Topiramate
- Zonisamide

Antiepileptic drugs can be classified according to their spectrum of action as:

Narrow spectrum

- Phenytoin
- Phenobarbital
- Carbamazepine
- Oxcarbazepine
- Gabapentin
- Pregabalin
- Lacosamide
- Vigabatrin

Broad spectrum

- Valproic acid
- Lamotrigine
- Topiramate
- Zonisamide
- Levetiracetam
- Clonazepam
- Rufinamide

Antiseizure medicines are the primary means of treating seizure clusters. The selection of these drugs differs according to semiology

and epileptic syndrome[40]. In October 2012, the Food and Drug Administration approved perampanel (Fycompa) as an additional antiseizure medication for the treatment of epilepsy with or without secondary generalization in patients aged 12 and up. In 60%-70% of individuals, carefully chosen antiepileptic medications give effective seizure control [41]. Pharmacologic treatment for seizure clusters comprises benzodiazepines, which are often well tolerated and serve as the foundation for cluster seizure treatment[32]. Because of their lipid solubility, they have a broad effectiveness spectrum and can penetrate the blood-brain barrier quickly [42]. Commonly documented adverse effects associated with benzodiazepines include lethargy, somnolence, and seldom respiratory depression; Benzodiazepine administration via intravenous (IV) or rectal routes has been linked to substantially higher incidence of respiratory adverse effects[43]. Benzodiazepines reduce seizures via activating GABAA receptors, leading to increased chloride conductance and hyperpolarization of the neuronal cell membrane. Although the fundamental mechanism of action for benzodiazepines is well defined, outcomes for individual therapy can differ in real world practise. Diazepam rectal gel was previously the sole treatment approved by the US FDA for increasing seizure activity in patients with epilepsy[44]. Other medications which are used to treat seizure clusters include sodium valproate, levetiracetam, phenytoin, carbamazepine, topiramate, lamotrigine, and oxcarbazepine. In actual practice, however, drugs via oral route (e.g., lorazepam) are frequently prescribed for acute rescue administration, particularly in teenagers and adults, where rectal treatments are generally unpopular.

According to the traditional medication system, for much of the last two decades (1997-2019), US Food and Drug Administration (FDA)-approved rescue medication was limited to rectal gel(diazepam), which was the first rescue medication approved for acute treatment of seizure clusters in patients over the age of two [45].However, the rectal route of drug delivery has mechanical limits (e.g., patient positioning and medicine administration) during a seizure, in addition to social and

privacy concerns [46].Oral administration of lorazepam and clonazepam, as well as intranasal delivery of atomized midazolam, are common instances of off-label therapy utilized as rescue medications for seizure clusters. Oral rescue medication administered when drowsy, particularly to individuals in the postictal state, may increase the risk of aspiration. Formulations administered buccal or sublingually have varying absorption and bioavailability [47]. Diazepam(IM) has also been demonstrated to be safe and beneficial in preventing seizure clusters[48]. Buccal midazolam was not approved or marketed in the USA, and diazepam via rectal route was the only approved treatment for cluster seizures[13]. Another factor which favors its use is the familiarity of the public with auto-injectors (e.g. EpiPen1) [49]. Adverse effects include local hematoma, discomfort, and the possibility of a caregiver needle puncture. Midazolam nasal spray is FDA-approved for treating seizure clusters in patients over 12 years old. The medicine comes in a single-use sprayer with a premeasured 5-mg dose (suitable for patients of various ages and weights).To control an ongoing cluster, apply a second dosage of midazolam nasal spray 10 minutes after the original dose. Patients at risk of respiratory depression should get a test dosage under the guidance of a healthcare practitioner. To ensure midazolam solubility, the formulation incorporates organic solvents such as ethanol, PEG-6, methyl ether, PEG-400, and propylene glycol. The most serious side events recorded with this medication were somnolence and nasal discomfort[50]. Various modes of administration for rescue therapy offer advantages and drawbacks[51]. Recently authorized intranasal formulations allow for faster administration than intravenous and rectal formulations. The approved intranasal midazolam formulations use organic solvents to improve solubility while maintaining a pH range of 5-9.7. However, the most common side effect recorded is nose discomfort[52]. Although intranasal administration of any drug is to provide rapid systemic and direct nose to brain exposure, here the potential role of mucociliary clearance should be taken into consideration. This physiological role helps to remove foreign particles from the nasal cavity to prevent them from

reaching the lungs. It has been suggested that a certain fraction of intranasally administered midazolam is absorbed via the GI tract, there is a 3.7%- 6.8% higher ratio of the metabolite 1- OH midazolam to midazolam after intranasal administration compared with intravenous administration.[53] Currently, it is unknown if this process is clinically relevant or whether the benzodiazepine rate or extent of absorption would be impacted if intranasal agents were administered to patients in the fed versus fasting state.

Future rescue therapies with different routes of administration and associated formulations are currently under investigation. Buccal diazepam film can be applied to the inner cheek, whereby the film dissolves and the diazepam is absorbed through the buccal mucosa. Buccal diazepam includes some of the similar beneficial characteristics as nasal spray benzodiazepines (e.g., avoids first - pass metabolism), while possessing some unique challenges in the mode of delivery (e.g., clenching of the jaw, drooling [54]. Furthermore, diazepam is not as efficiently absorbed via the digestive system as it is through the buccal mucosa [55] when taken. Inhaled alprazolam is an investigational medication that takes advantage of the lung architecture (big surface area, broad blood supply) to administer the drug and increase absorption rates. In a proof-of-concept trial, inhaled alprazolam reduced epileptiform activity in photosensitive patients, with effectiveness reported 2 min after delivery [56].

Rescue therapies should have high efficacy, fast absorption, constant bioavailability, and a broad therapeutic index. The efficiency of drug distribution depends on the route of administration and formulation, with significant variances between rescue regimens. Effective rescue therapies need prompt measures from patients, family members, and caregivers, as well as education and an acute seizure action plan [57].

In conclusion, benzodiazepines remain the primary treatment for seizure clusters. New routes of administration have been approved,

while others are currently being investigated. Each method of administration has its own advantages and disadvantages that make it acceptable or desirable for some patients. Each patient should have a seizure action plan that includes rescue therapy for seizure clusters, as well as details on when to deliver treatment and what drug and dose to use. Patients and caregivers must be counselled and instructed on how to administer rescue treatment. Early treatment outside the hospital reduces morbidity and mortality in seizure clusters, lowers treatment costs, and enhances the life’s quality for patients and their families.

MATERIALS AND METHODS

SOURCE OF DATA

This study was conducted in patients with epilepsy who attended epilepsy clinic OPD at Dayanand Medical Hospital in Ludhiana city.

METHODS OF COLLECTION OF DATA

Consenting patients / assenting children and their parents attending Neurology/Epilepsy clinic who fulfilled all the inclusion criteria and none of the exclusion criteria were included in the study.

INCLUSION CRITERIA

1) Age: Any

2) Gender: either

3) Known case of epilepsy on Anti-epileptic drugs

4) Subjects reporting >3 seizures in 24 hours

5) Co-morbid conditions: Any

EXCLUSION CRITERIA

1) Non epileptic seizures

2) Non consenting patients

STUDY DESIGN

This was a three year retrospective study and one year prospective study in which patients having seizure clusters (who were initiated on treatment or being treated with Anti seizure medications) were enrolled. Patients were asked to maintain a seizure diary and follow up of 3 months.

DURATION OF STUDY

This study was conducted for total duration of 4 Years (3 year retrospective and 1 year prospective study)

15th September 2019 - 14th September 2022(Retrospective date)

15th September 2022 - 14th September 2023(Prospective date)

OUTCOME PARAMETERS

Assessment of incidence of cluster seizures among cohort of patients with epilepsy.

Assessment of efficacy, safety and tolerability of pharmacological options used for management of cluster seizures based on seizure semiology, frequency and control of seizures.

Methodology

After obtaining clearance from Institutional Ethics Committee, the consenting patients were enrolled on OPD basis that fulfilled all the inclusion criteria. Patient demographics i.e. Gender, age, family history, residential area along with clinical characteristics such as history of past and present seizures, clusters, ASMs treatment and other concomitant treatment were recorded. Patients were started on antiseizure medications with optimization of drugs and dose according to seizure semiology in their subsequent visits during follow up period of 3 months.

According to the history narrated by the patients/attendants, seizure semiology was identified and seizure cluster frequency was noted. Adverse drug reaction (ADR) caused by drugs were noted. Causality assessment was done using WHO-UMC scale.

Incidence of seizure clusters was calculated by: Number of patients with seizure clusters / Total number of people enrolled with epilepsy. Their incidence was calculated based on their semiologies.

STATISTICAL ANALYSIS

The obtained results were entered in Microsoft excel and analysed using descriptive statistics.

OBSERVATIONS AND RESULTS

Figure 1: Consort flowchart

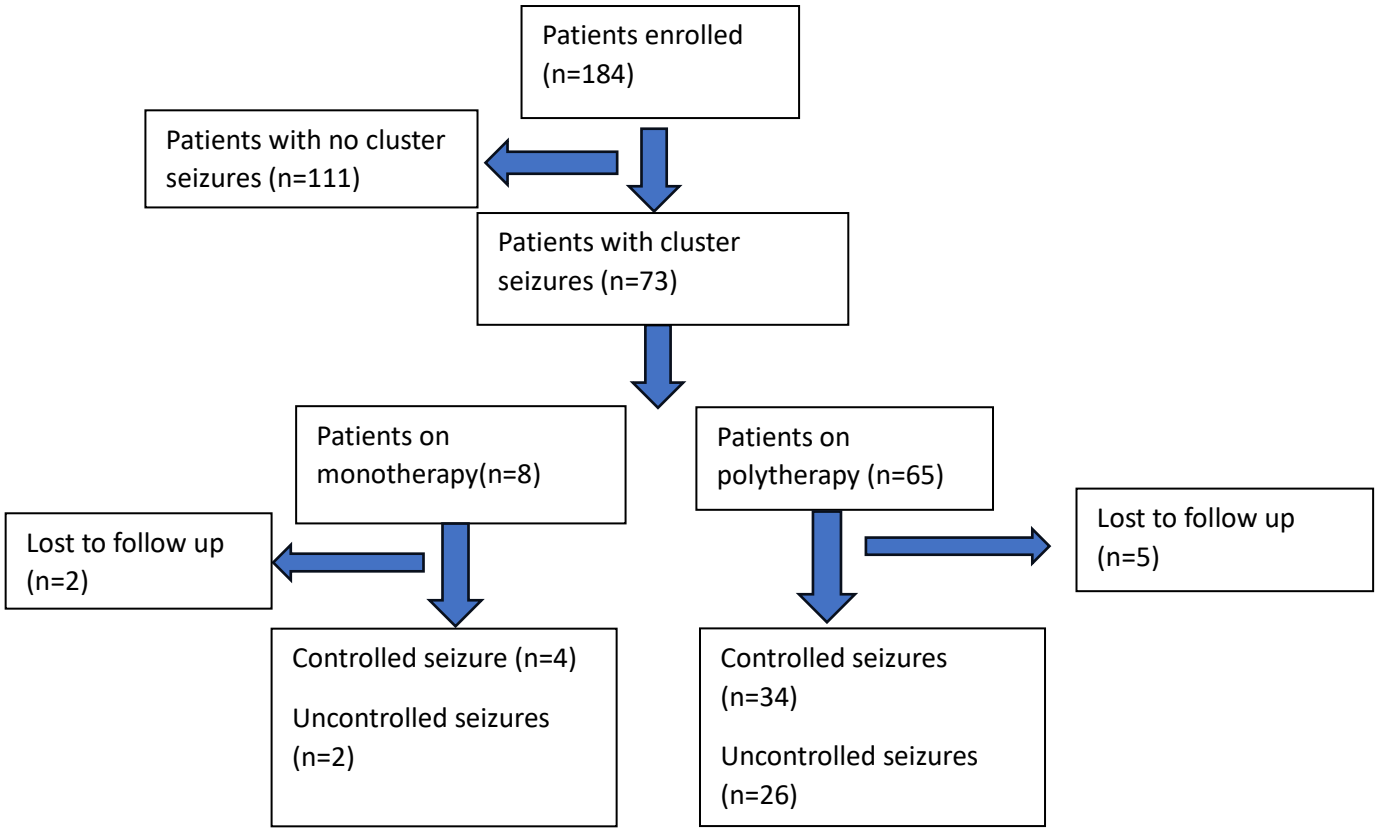

Figure 2: Incidence of cluster seizures among cohort of people with epilepsy (n=184)

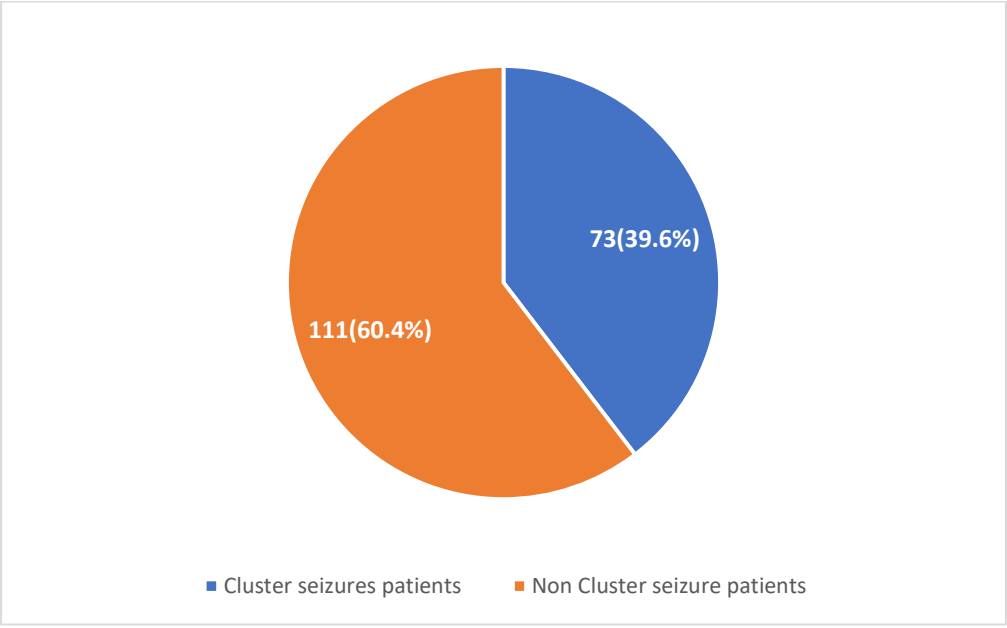

Figure 3: Incidence of various semiologies in patients with clustered seizures (n=66)

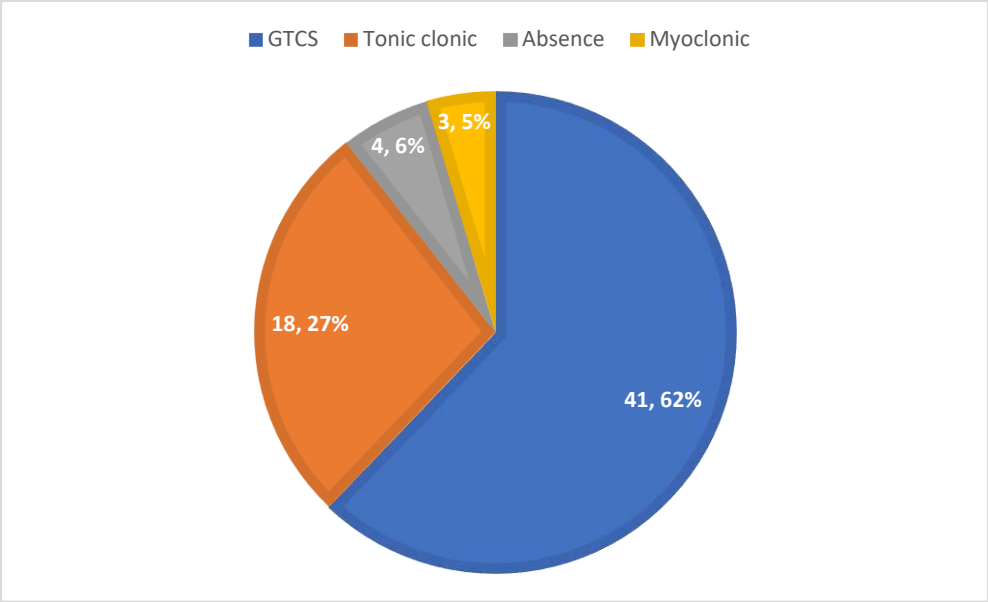

Table 1: Distribution of patients with seizure clusters based on age group (n=66)

Age group (n)	Seizure semiology (n)	Fischer's exact value	P value
0-10 years (14)	• GTCS (8) • Tonic clonic (5) • Myoclonic (1)	9.52	0.08
11-20 years (17)	• GTCS (9) • Tonic clonic (5) • Absence (2) • Myoclonic (1)		
21-30 years (20)	• GTCS (13) • Tonic clonic (5) • Myoclonic (1) • Absence (1)		
31-40 years (8)	• GTCS (6) • Tonic clonic (2)		
41-50 years (6)	• GTCS (4) • Absence (1) • Tonic clonic (1)		
>50 years (1)	• GTCS (1)		

Table 2: Distribution of patients with seizure clusters based on gender (n=66)

Gender distribution (n)	Semiology (n)	Chi square value	P value
Female (29)	• GTCS (20) • Tonic clonic (6) • Absence (2) • Myoclonic (1)	2.01	0.15
Male (37)	• GTCS (21) • Tonic clonic (12) • Absence (2) • Myoclonic (2)		

Figure 4: Gender distribution of patients with GTCS semiology (n=41)

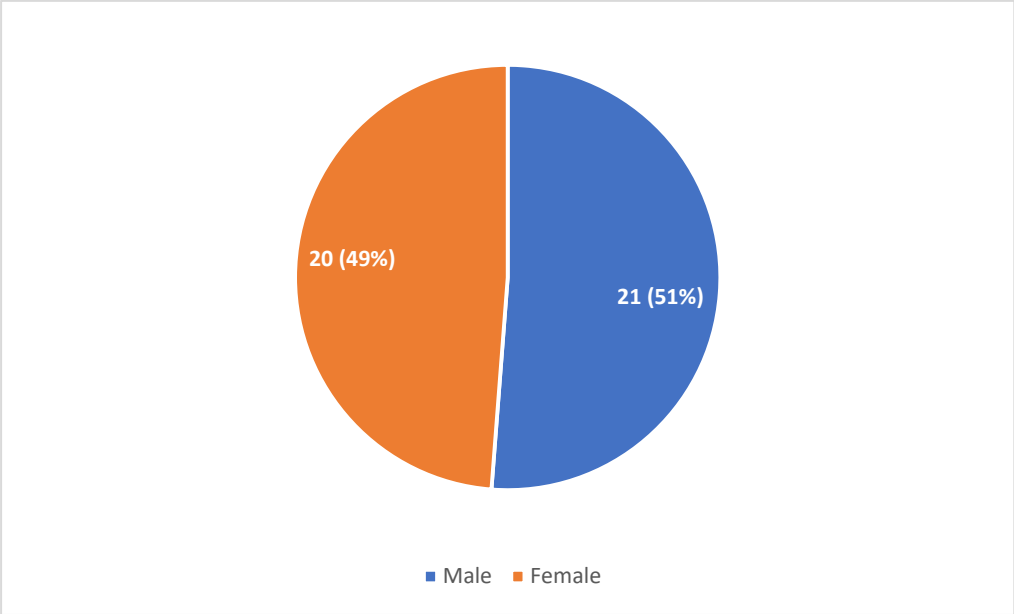

Figure 5: Gender distribution of patients with tonic clonic semiology (n=18)

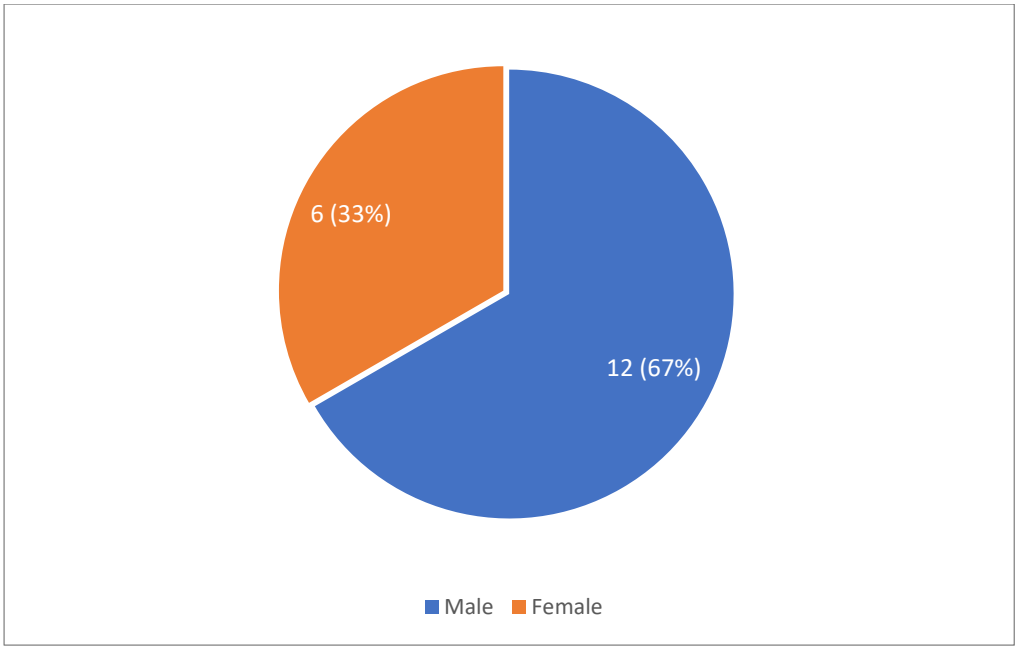

Figure 6: Gender distribution of patients with Absence semiology (n=4)

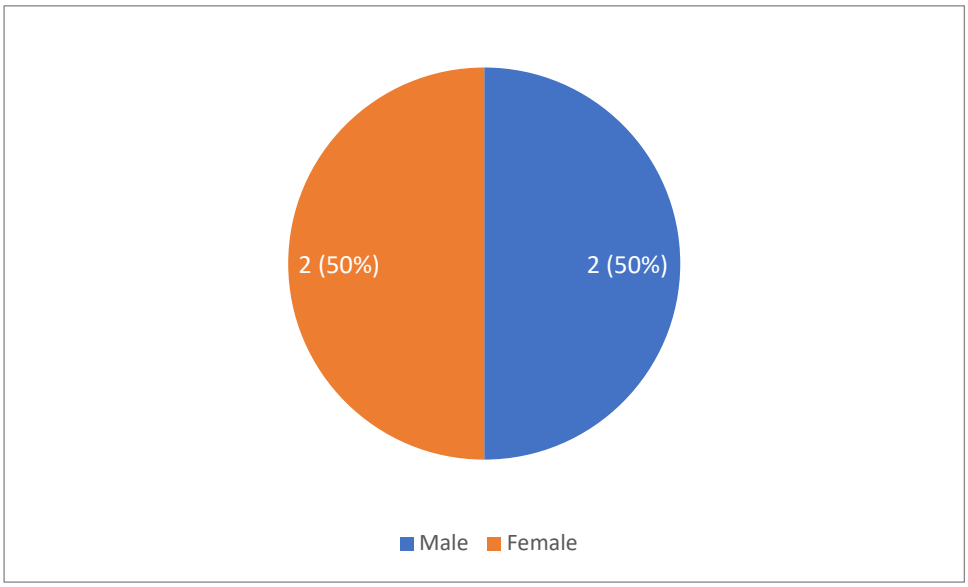

Figure 7: Gender distribution of patients with Myoclonic semiology (n=3)

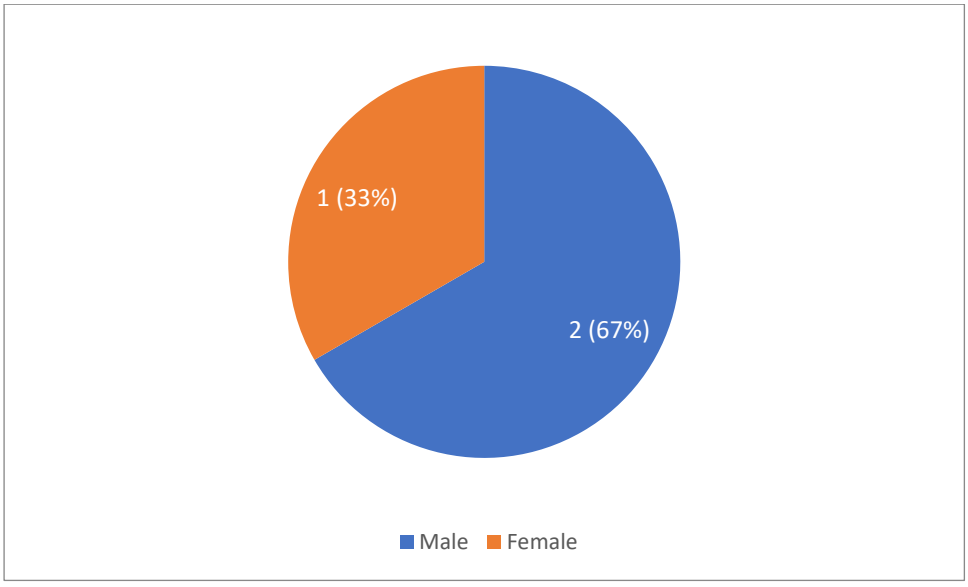

Table 3: Distribution of patients with seizure cluster based on residential area (n=66)

Residential area (n)	Seizure semiology	Chi square value	p value
Rural (43)	• GTCS (26) • Tonic clonic (11) • Myoclonic (2) • Absence (4)	0.15	0.69
Urban (23)	• GTCS(14) • Tonic clonic(7) • Myoclonic(1) • Absence(1)		

Table 4: Distribution of patients with seizure cluster based on family history (n=66)

Family history (n)	Seizure semiology(n)	Chi square vale	P value
Positive(24)	• GTCS (8) • Tonic clonic (13) • Absence(2) • Myoclonic(1)	12.58	0.001
Negative (42)	• GTCS(33) • Tonic clonic (5) • Absence (2) • Myoclonic (2)		

Table 5: Association between family history and semiology

	Semiology				Chi square value	P value
	Tonic clonic	GTCS	Absence	Myoclonic		
Positive (n=24)	13 (54.2%)	8 (33.3%)	2(8.3%)	1(4.2%)	15.36	0.002
Negative (n=42)	5 (12%)	33(78.6%)	2(4.8%)	2(4.8%)		

Figure 8: Family history based distribution of patients with cluster seizures (n=66)

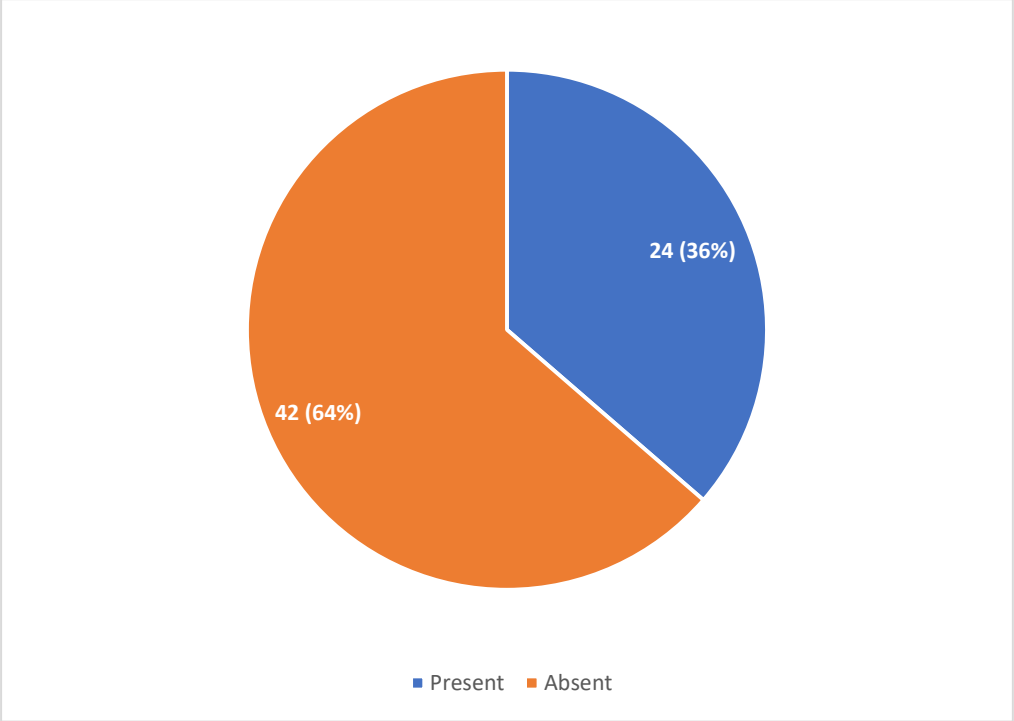

Figure 9: Risk factors for development of seizure clusters (n=66)

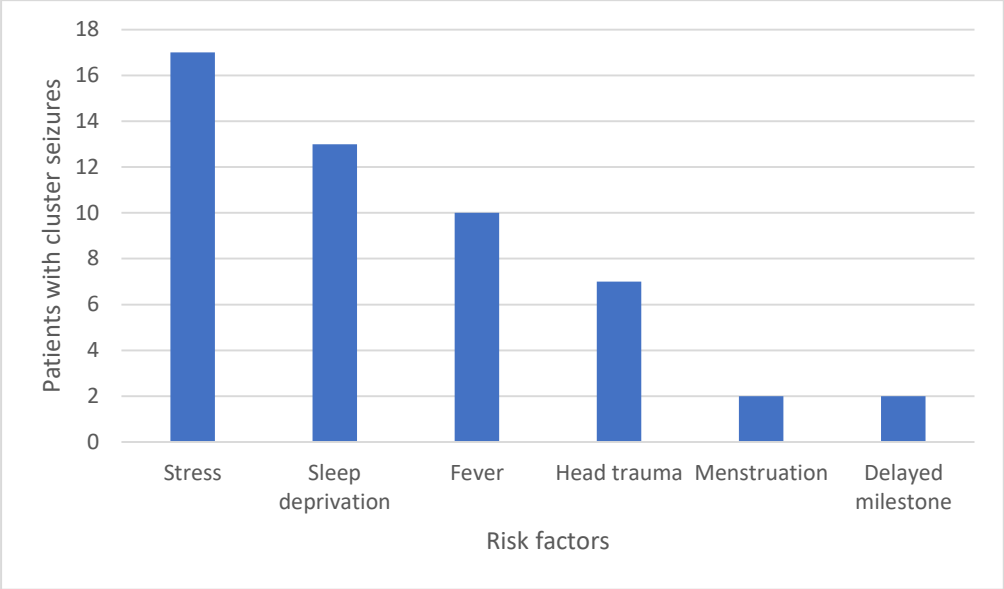

Figure 10: Risk factors for development of seizure clusters in patients with GTCS semiology

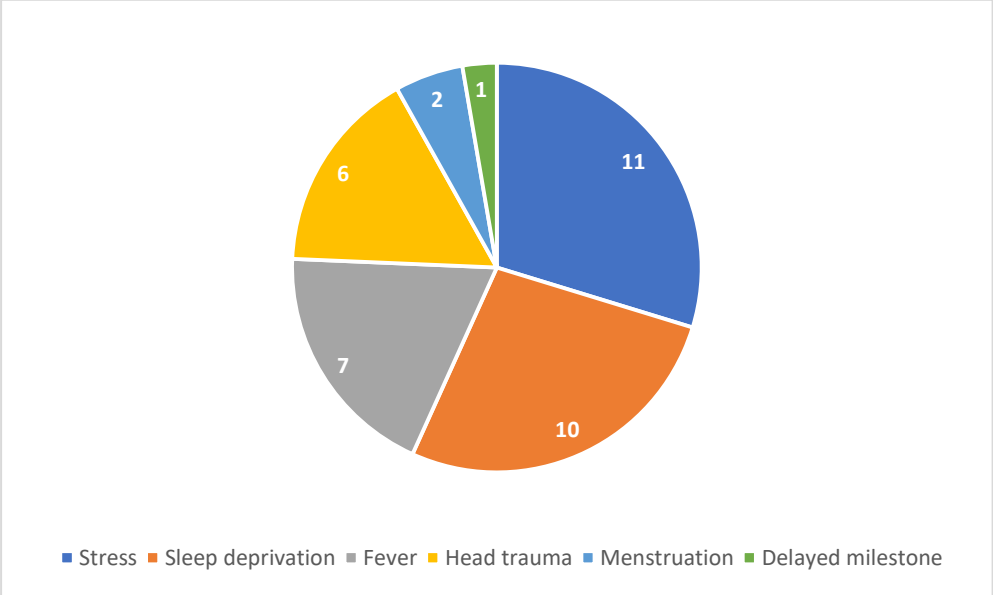

Figure 11: Risk factors for development of seizure clusters in patients with tonic clonic semiology

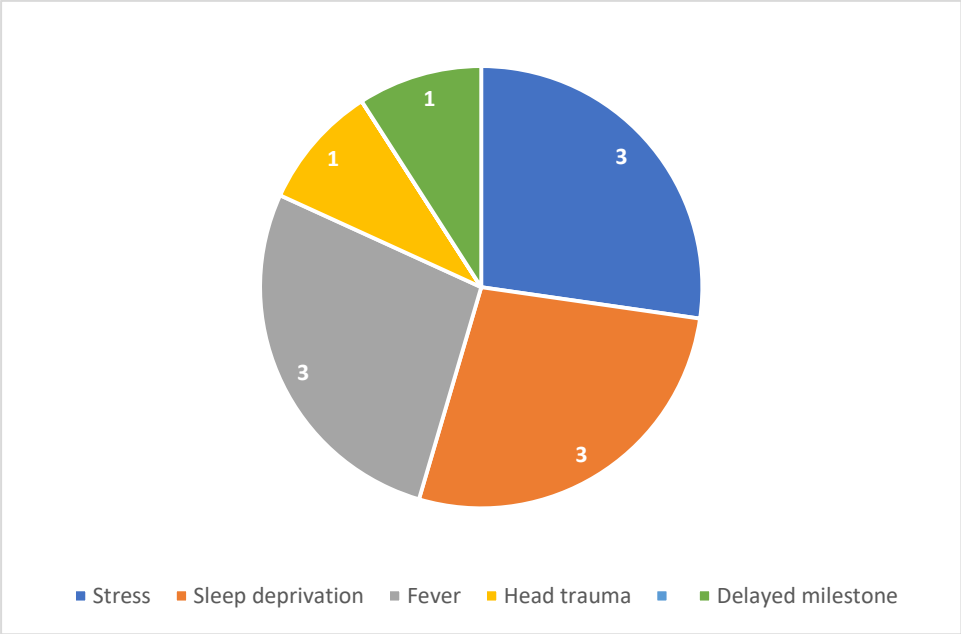

Table 6: Distribution of patients based on frequency of seizures in a cluster (n=66)

Seizure semiology (n)	4-5 seizures	6-10 seizures	>10 seizures
Tonic clonic (18)	16	2	0
GTCS (41)	29	11	1
Absence (4)	4	0	0
Myoclonic (3)	2	1	0

Table 7: Association between seizure cluster and structural lesion in MRI

		Seizure cluster					chi square value	P value
		Yes		No		Total	5.93	0.01
		n	%	n	%			
MRI	Abnormal	10	41.7%	13	58.3%	23		
	Normal	21	19.6%	86	80.4%	107		

Table 8: Control of Seizure clusters in patients with focal epilepsy having structural lesions in MRI

Structural lesion	Semiology	No of seizure clusters	Intervention	seizure cluster control	
				Yes	No
MTS	Tonic clonic (n=3)	4 5 4	Levetiracetam+ sodium valproate* Oxcarbazepine+ brivaracetam*+ divalproex Carbamazepine+ levetiracetam+ oxcarbazepine+ lacosamide@+clobazam*	+ + +	- - -

#addition of drug, *increase in dose, $stop of drug, @decrease in dose

Table 9: Control of Seizure clusters in patients with Generalized epilepsy having structural lesions in MRI

Structural lesion	Semiology (n)	No of seizure clusters	Intervention	seizure cluster control	
				Yes	No
MTS	GTCS (3)	5	Levetiracetam+oxcarbazepine*	+	-
		4	Sodium valproate+ carbamazepine+ levetiracetam*	+	-
		4	Sodiumvalproate+ levetiracetam+ phenytoin+ carbamazepine#	-	+
	Myoclonic (n=1)	6	Sodium valproate*+ carbamazepine$+ topiramate+ clobazam	-	+
Cerebral atrophy	GTCS(2)	7	Sodium valproate*+ carbamazepine+ lamotrigine	+	-
		5	Carbamazepine*+levetiracetam	+	-
Calcified granuloma	GTCS(1)	5	Sodium valproate*+ Oxcarbazepine	-	+

Table 10: Association between seizure cluster and EEG changes

		Seizure cluster					chi square value	P value
		Yes		No		Total		
		n	%	n	%		0.00	0.99
EEG lesion	Abnormal	15	24.6%	46	75.4%	61		
	Normal	17	24.6%	52	75.4%	69		

Table 11: Control of seizure clusters in patients with focal epilepsy having EEG changes

EEG changes	semiology	No of seizure clusters	Intervention	seizure cluster control	
				Yes	No
Focal epileptiform activity arising from frontal lobe	Tonic clonic (n=1)	4	Levetiracetam+carbamazepine*	-	+

#addition of drug, *increase in dose, $stop of drug, @decrease in dose

Table 12: Control of seizure clusters in patients with generalized epilepsy having EEG changes

EEG changes	Semiology	No of seizure clusters	Intervention	seizure cluster control	
				Yes	No
Focal epileptiform activity arising from frontal lobe	GTCS (n=3)	7	Sodium valproate*+ carbamazepine + lamotrigine	+	-
		4	Sodium valproate+ ethosuximide+ lamotrigine*	+	-
		4	Oxcarbazepine+ phenobarbitone*+ lamotrigine+ clobazam@	-	+
	Absence (n=1)	4	Levetiracetam*+ oxcarbazepine	-	+
	Myoclonic (n=1)	6	Sodium valproate*+ carbamazepine$+ topiramate+clobazam	-	+
Interictal records of Idiopathic generalized seizures	GTCS (n=3)	4	Sodium valproate+ levetiracetam*	+	-
		4	Levetiracetam+ sodium valproate*+ phenobarbitone+ clobazam	+	-
		4	Valproic acid+ levetiracetam+ carbamazepine*+brivaracetam+ clobazam	+	-
	Absence (n=1)	5	Sodium valproate*	+	-
	Myoclonic (n=1)	5	Sodium valproate*	+	-
Focal epileptiform activity arising from Right parieto temporal lobe	GTCS (n=3)	3	Carbamazepine+ levetiracetam*+ divalproex+ clobazam	+	-
		3	Sodium valproate+ carbamazepine+ levetiracetam*	+	-
		3	Carbamazepine+ levetiracetam+ lacosamide*+ clobazam	-	+
Focal epileptiform activity arising from occipital lobe	GTCS (n=1)	6	Oxcarbazepine*+brivaracetam#+ lamotrigine	+	-

#addition of drug, *increase in dose, $stop of drug, @decrease in dose

Table 13: Seizure cluster control in patients with combined MRI lesions & EEG changes

Structural lesion	EEG changes	semiology	No of seizure clusters	Intervention	seizure cluster control	
					Yes	No
MTS	Interictal records of Idiopathic generalized seizures	GTCS	4	Sodium valproate+ carbamazepine+ levetiracetam*	+	-
MTS	Focal epileptiform activity arising from frontal lobe	Myoclonic	6	Sodium valproate*+ carbamazepine$+ topiramate+ clobazam	-	+
Cerebral atrophy	Focal epileptiform activity arising from frontal lobe	GTCS	7	Sodium valproate*+ carbamazepine+ lamotrigine+ clobazam#	+	-

#addition of drug, *increase in dose, $stop of drug, @decrease in dose

Table 14: Control of seizure cluster in patients on Monotherapy (n=6)

Semiology	No of patients	Drug used	Seizure cluster control	
			Yes	No
GTCS	2	• Carbamazepine	+	+
	1	• Levetiracetam	+	-
	1	• Oxcarbazepine*	+	-
Absence	1	• Sodium valproate*	+	-
Myoclonic	1	• Sodium valproate*	-	+

#addition of drug, *increase in dose, $stop of drug, @decrease in dose

Table 15: Control of seizure clusters in patients on polytherapy with GTCS semiology (n=37)

Primary drug Carbamazepine (n=8)	No of patients	Seizure cluster control	
		Yes	No
1. Carbamazepine* + phenytoin	1	+	-
2. Carbamazepine+ divalproex+ levetiracetam+ clobazam*	1	+	-
3. Carbamazepine* +phenobarbitone+ lamotrigine+ phenytoin+ clobazam	1	+	-
4. Carbamazepine+ topiramate+ clobazam@	1	-	+
5. Carbamazepine+ sodium valproate*+ clobazam*	1	-	+
6. Carbamazepine+ levetiracetam+ phenobarbitone*	1	-	+
7. Carbamazepine+ brivaracetam+ permapanel$+ clobazam	1	-	+
8. Carbamazepine+ levetiracetam+ lacosamide*+ clobazam	1	-	+
Total	8		

#addition of drug, *increase in dose, $stop of drug, @decrease in dose

Primary drug Sodium valproate (n=14)	No. of patients	Seizure cluster control	
		Yes	No
1. Sodium valproate*+ lamotrigine	1	+	-
2. Sodium valproate+ levetiracetam*	1	+	-
3. Sodium valproate+ lamotrigine*+ ethosuximide	1	+	-
4. Sodium valproate + lacosamide*+ lorazepam	1	+	-
5. Sodium valproate + oxcarbazepine#+ clobazam	1	+	-
6. Sodium valproate+ levetiracetam* + lacosamide	1	+	-
7. Sodium valproate*+ lamotrigine+ clobazam@	1	+	-
8. Sodium valproate+ levetiracetam*+ carbamazepine+ clobazam#	1	+	-
9. Sodium valproate+ phenytoin+ carbamazepine#+ levetiracetam	1	+	-
10. Sodium valproate+brivaracetam +levetiracetam+carbamazepine*+ clobazam	1	+	-
11. Sodium valproate* +oxcarbazepine	1	-	+
12. Sodium valproate+Phenytoin*	1	-	+
13. Sodium valproate+Lamotrigine*	1	-	+
14. Sodium valproate*+ lamotrigine+ carbamazepine+ clobazam#	1	-	+
Total	14		

#addition of drug, *increase in dose, $stop of drug, @decrease in dose

Primary drug Levetiracetam (n=7)	No. of patients	Seizure cluster control	
		Yes	No
1. Levetiracetam+oxcarbazepine*	1	+	-
2. Levetiracetam+sodium valproate$+phenytoin#	1	+	-
3. Levetiracetam+carbamazepine*+clobazam	1	+	-
4. Levetiracetam+carbamazepine*+clobazam	1	+	-
5. Levetiracetam +sodium valproate*+ phenobarbitone +clobazam	1	+	-
6. Levetiracetam* +Clonazepam	1	-	+
7. Levetiracetam+ Carbamazepine*	1	-	+
Total	7		

#addition of drug, *increase in dose, $stop of drug, @decrease in dose

Primary drug Oxcarbazepine (n=5)	No. of patients	Seizure cluster control	
		Yes	No
1. oxcarbazepine+ Clobazam@	1	+	-
2. oxcarbazepine*+ lamotrigine+ brivaracetam#	1	+	-
3. oxcarbazepine+ Clobazam*	1	-	+
4. oxcarbazepine+ phenobarbitone*+ lamotrigine+ clobazam#	1	-	+
5. oxcarbazepine+ phenytoin+ phenobarbitone*+ clobazam	1	-	+
Total	5		

#addition of drug, *increase in dose, $stop of drug, @decrease in dose

Primary drug Phenytoin (n=3)	**No. of patients**	**Seizure cluster control**	
		Yes	**No**
1. Phenytoin+ clobazam*	1	+	-
2. Phenytoin*+ clobazam	1	-	+
3. Phenytoin+ levetiracetam+ clobazam#	1	-	+
Total	3		

#addition of drug, *increase in dose, $stop of drug, @decrease in dose

Table 16: Control of seizure clusters in patients on polytherapy with tonic clonic semiology (n=18)

Primary drug Carbamazepine (n=4)	No. of patients	Seizure cluster control	
		Yes	No
1. Carbamazepine + sodium valproate$+ Clobazam	1	+	-
2. Carbamazepine+ levetiracetam+ lacosamide@+ clobazam*	1	+	-
3. Carbamazepine+ phenytoin+ phenobarbitone*+ clobazam#	1	+	-
4. Carbamazepine* + Levetiracetam	1	-	+
Total	4		

#addition of drug, *increase in dose, $stop of drug, @decrease in dose

Primary drug Levetiracetam (n=4)	No. of patients	Seizure cluster control	
		Yes	No
1. Levetiracetam+ Carbamazepine+ sodium valproate*	1	+	-
2. Levetiracetam*+ phenytoin+ clobazam	1	+	-
3. Levetiracetam+ sodium valproate+ Perampanel+ clobazam*	1	+	-
4. Levetiracetam+ Carbamazepine#+ clobazam	1	-	+
Total	4		

#addition of drug, *increase in dose, $stop of drug, @decrease in dose

Primary drug Oxcarbazepine (n=7)	No.of patients	Seizure cluster control	
		Yes	No
1. Oxcarbazepine*+sodium valproate	1	+	-
2. Oxcarbazepine*+ brivaracetam+ divalproex	1	+	-
3. Oxcarbazepine +levetiracetam@+ lacosamide	1	+	-
4. Oxcarbazepine+ levetiracetam$+ Clobazam*	1	-	+
5. Oxcarbazepine+ topiramate*+ Clobazam	1	-	+
6. Oxcarbazepine+ Sodium valproate*+ topiramate	1	-	+
7. Oxcarbazepine+ Phenytoin*+ lacosamide*	1	-	+
Total	7		

#addition of drug, *increase in dose, $stop of drug, @decrease in dose

Primary drug Sodium valproate(n=2)	No. of patients	Seizure cluster control	
		Yes	No
1. Sodium valproate* + Levetiracetam	1	+	-
2. Sodium valproate+ levetiracetam* + Clobazam	1	+	-
Total	2		

#addition of drug, *increase in dose, $stop of drug, @decrease in dose

Primary drug Phenobarbitone(n=1)	No. of patients	Seizure cluster control	
		Yes	No
1. Phenobarbitone +vigabatrin+ levetiracetam+ sodium valproate# Clobazam@	1	-	+
Total	1		

#addition of drug, *increase in dose, $stop of drug, @decrease in dose

Table 17: Control of seizure clusters in patients on polytherapy with absence semiology (n=3)

Primary drug Levetiracetam (n=2)	No. of patients	Seizure cluster control	
		Yes	No
1. Levetiracetam+ Carbamazepine*	1	+	-
2. Levetiracetam*+ Oxcarbazepine	1	-	+
Total	2		

#addition of drug, *increase in dose, $stop of drug, @decrease in dose

Primary drug Brivaracetam (n=1)	No. of patients	Seizure cluster control	
		Yes	No
1. Brivaracetam+ Carbamazepine*+ clobazam	1	-	+
Total	1		

#addition of drug, *increase in dose, $stop of drug, @decrease in dose

Table 18: Control of seizure clusters in patients on polytherapy with myoclonic semiology (n=2)

Primary drug Sodium valproate(n=2)	No of patients	Seizure outcome control	
		Yes	No
1. sodium valproate+ levetiracetam+ Clobazam*	1	+	-
2. sodium valproate*+ Carbamazepine$+ topiramate+ clobazam	1	-	+
Total	1		

#addition of drug, *increase in dose, $stop of drug, @decrease in dose

Table 19: Intervention strategies which resulted in control of seizures across various semiologies

Intervention	Increase in dose	Add on drug	Decrease in dose	Discontinuation of drug
Clobazam	5	2	2	0
Levetiracetam	5	0	1	0
Sodium valproate	5	0	0	2
Carbamazepine	6	1	0	0
Oxcarbazepine	4	1	0	0
Phenytoin	0	1	0	0
Lamotrigine	1	0	0	0
Phenobarbitone	1	0	0	0
Lacosamide	1	0	1	0
Brivaracetam	0	1	0	0

Table 20: Semiology wise distribution of patients who were lost to follow up (n=7)

Semiology	No of patients	Combinations of drugs used
GTCS	1 1 1	• Sodium valproate+carbamazepine* • Phenytoin+Levetiracetam+ clobazam • Sodium valproate*+Oxcarbazepine
Tonic clonic	1 1 1	• Carbamazepine+levetiracetam • Phenytoin+carbamazepine+clobazam • Brivaracetam
Absence	1	• Phenobarbitone

#addition of drug, *increase in dose, $stop of drug, @decrease in dose

Figure-12: Pattern of Anti seizure medications used in people with epilepsy having seizure clusters (n=66)

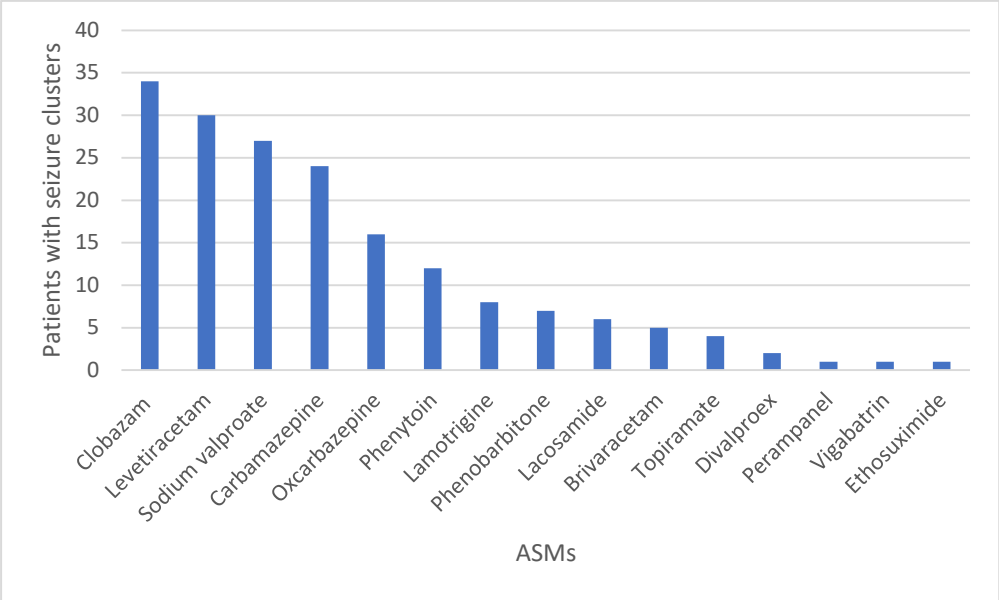

Figure 13: Pattern of Adverse drug reactions reported in patients with cluster seizures

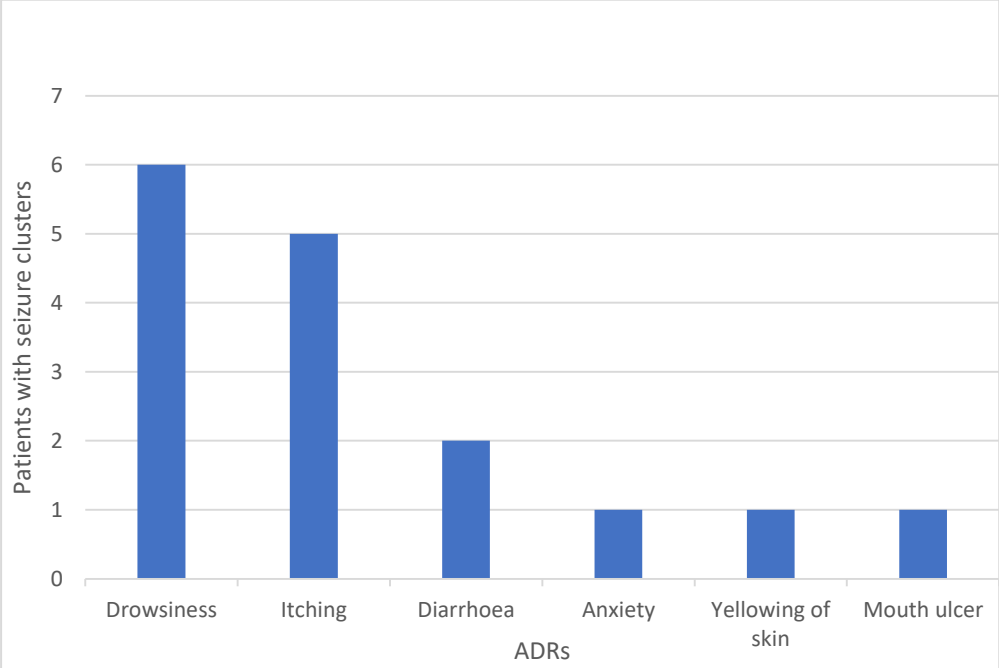

Figure 14: Drug wise pattern of ADRs with different Anti seizure medications

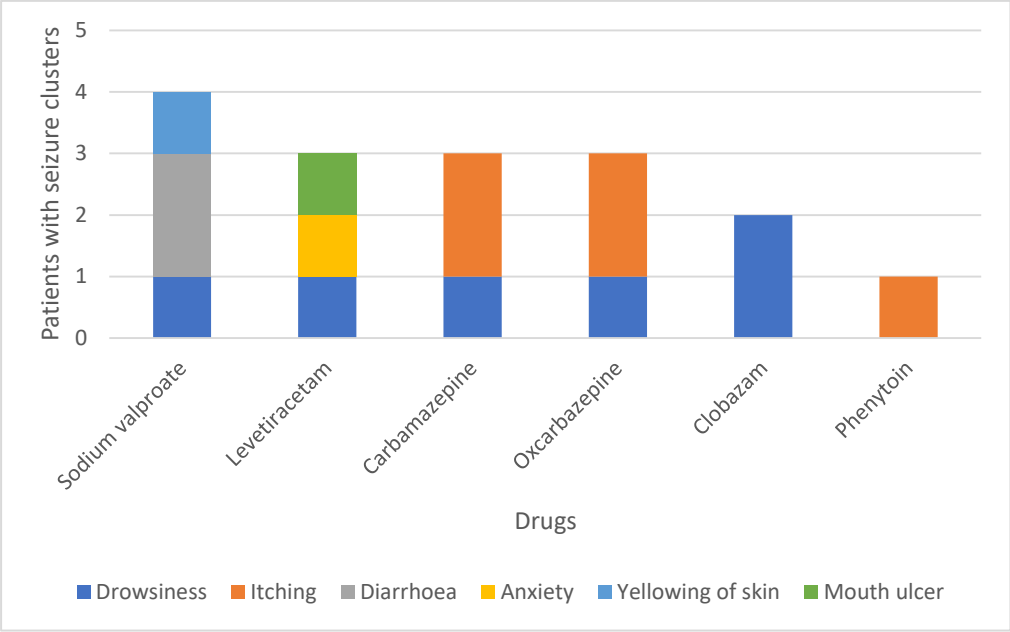

Figure 15: Pattern of ADRs reported with different Anti seizure medications

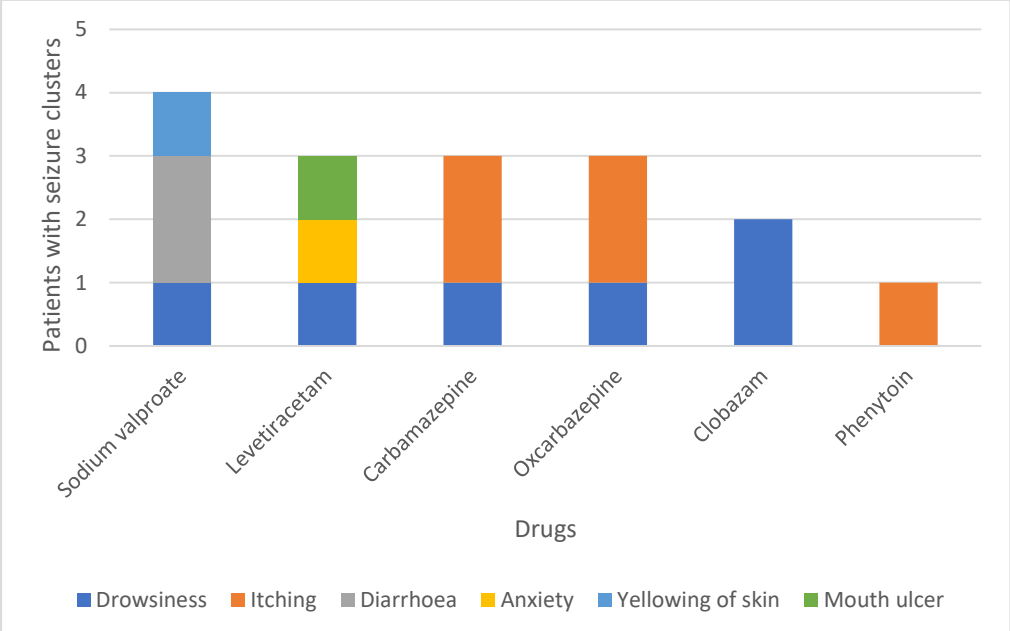

Table 21: Causality assessment of ADRs

ADR	Anti seizure medication	Causality assessment
Drowsiness(n=6)	Sodium valproate(n=1) Levetiracetam (n=1) Carbamazepine(n=1) Oxcarbazepine(n=1) Clobazam(n=2)	Possible Possible Possible Possible Possible
Itching (n=5)	Carbamazepine(n=2) Oxcarbazepine(n=2) Phenytoin(n=1)	Possible Possible Possible
Diarrhoea(n=2)	Sodium valproate(n=2)	Possible
Mouth ulcer(n=1)	Levetiracetam(n=1)	Certain
Anxiety (n=1)	Levetiracetam(n=1)	Possible
Yellowing of skin(n=1)	Sodium valproate(n=1)	Probable

RESULTS

This was an observational study conducted in consenting people with epilepsy in the cohort of patients presenting to epilepsy clinic, DMCH Ludhiana. Patients who fulfilled to inclusion criteria, a written informed consent was taken. The study was started after taking approval from Institutional Ethics Committee. A total of 184 patients were enrolled out of which 83 patients were identified from records (retrospective data) and 101 patients were enrolled prospectively. Out of 184 enrolled patients, 73 had cluster seizures with 44 patients who presented with GTCS semiology, 21 patients with tonic clonic semiology, 5 patients with absence semiology and 3 patients with myoclonic semiology. However, 7 patients were lost to follow up therefore data of 66 patients was analyzed.(figure 1)

The seizure clusters in our study were defined as patients reporting more than 3 seizures in a day. Incidence of clustered seizures was 39.6% among cohort of people with epilepsy (figure2).Patients with GTCS semiology had the incidence of 62% (n=41). Patients with tonic clonic semiology had the incidence of 27% (n=18). Patients with absence semiology had incidence of 6% (n=4) and the incidence among patients with myoclonic semiology was 5% (n=3) (figure 3).

Patient demographics i.e. age, gender along with clinical characteristics such as history of present treatment and other concomitant treatment were recorded in a semi structured proforma. The study subjects were started on antiseizure medications (ASMs) according to their seizure semiology. They were asked to maintain a seizure diary follow up for 3 months.

Most of the patients with clustered seizures belong to age group of 21-30 years which included GTCS (n=13), tonic clonic (n=5) absence and myoclonic each (n=1) followed by 11-20 years of age with GTCS (n=10), tonic clonic (n=5), absence (n=2) and myoclonic (n=1).Patients in age group 0-10 were 14 with GTCS (n=8) tonic clonic (n=5) and myoclonic (n=1), there was no absence semiology patient reported in

this age group. Patients in the age group of 31-40 were GTCS (n=6) and tonic clonic (n=2). Patients in 41-50 age group were GTCS (n=6), absence (n=1), tonic clonic (n=1) and least being in the elderly age group >50 with GTCS semiology (n=1) (table 1) (p=0.08).

Among these patients 29 were females (p=0.93) with more number with GTCS (n=20), tonic clonic (n=6), absence (n=2) and myoclonic (n=1); and 37 were males with GTCS (n=21), tonic clonic (n=12), absence (n=2) and myoclonic (n=2) (table2) (figure 4-7)

Most of the study population belonged to rural areas (n=43, 65.2%) among which patient semiology was GTCS (n=26), tonic clonic (n=11), absence (n=4) and myoclonic (n=2) and patients from urban population were (n=23, 34.8%) with more number of patients presenting with semiology GTCS (n=14) followed by tonic clonic (n=7), myoclonic (n=1) and absence (n=1) (p=0.69) (table 3)

Family history of epilepsy was absent in 42 patients with GTCS(n=33), tonic clonic (n=5), absence(n=2) and myoclonic(n=2) and present in 24 patients with semiology as tonic clonic (n=13), GTCS (n=8),absence (n=2) and myoclonic (n=1) (p=0.001) which depicts the association between absence of positive family history and seizure cluster(table 4) (figure 8).

There was significant association observed between absence of positive family history and GTCS semiology (p=0.002) (table 5)

Most common risk factors for the development of seizure clusters in our study were stress (n=17) in patients with GTCS (n=11), absence (n=3), tonic clonic (n=3) semiology. Sleep deprivation (n=13) was seen in GTCS (n=10) and tonic clonic (n=3) semiology. Fever (n=10) in patients with GTCS (n=7), tonic clonic seizures (n=3). Head trauma (n=7) with GTCS (n=6) and tonic clonic (n=1) semiology. Menstruation (n=2) with GTCS. Delayed milestones (n=2) with GTCS (n=1) and tonic clonic (n=1).(figure 9,10,11)

There were more number of patients of 4-5 clusters with GTCS (n=29) followed by tonic clonic seizures (n=16), absence seizures (n=4) and myoclonic seizures (n=2). Patients who reported with 6-10 clustered seizures had GTCS (n=11), tonic clonic semiology (n=2) and myoclonic (n=1). Patients with GTCS semiology who had more than 10 clustered seizures were (n=1). (table6)

There were statistically significant results observed between absence of MRI structural lesion in MRI and seizure clusters (p=0.01) (table 7). Abnormal MRI lesions were reported in ten patients with seizure clusters. All three patients with focal epilepsy had MTS as structural lesion and their seizure clusters were controlled on different regimens. One patient was on levetiracetam & sodium valproate, when the dose of sodium valproate was increased his clusters were controlled. Another patient was on combination of oxcarbazepine, brivaracetam and divalproex, when the dose of brivaracetam was increased his clusters were controlled. In the third patient, who was on combination of carbamazepine, levetiracetam, oxcarbazepine, lacosamide and clobazam, when the dose of clobazam was increased and lacosamide was decreased cluster seizures were controlled. (table 8)

Among patients of generalized epilepsy, three patients with GTCS who had MTS as structural lesion. Among them only 2 patients clustered seizures were controlled. One patient was on combination of levetiracetam and oxcarbazepine. When the dose of oxcarbazepine was increased, clustered seizures were controlled. Second patient was on combination of sodium valproate, carbamazepine and levetiracetam when the dose of levetiracetam was increased the patient's seizures was controlled. There were 2 patients of cerebral atrophy with GTCS semiology who had their seizure clusters controlled with various combinations. The first patient who had 7 clustered seizures daily was on drug combinations of sodium valproate, carbamazepine& lamotrigine. After increasing the dose of sodium valproate, the patient seizure clusters were controlled. Second patient with 5 seizures per day was on combination of carbamazepine & levetiracetam, when the

dose of carbamazepine was increased the patient seizures were controlled.(table 9). However the patient with calcified granuloma who was on combination of sodium valproate and oxcarbazepine, despite increasing the dose of sodium valproate seizure clusters were not controlled.

There was no association observed between seizure cluster and positive EEG findings (p=0.99) (table 10). EEG findings were observed in 15 patients with seizure clusters. Patient of focal epilepsy with focal epileptiform activity arising from frontal lobe did not result in seizure control with dose modification (table 11).

There were 14 patients with generalized epilepsy who had EEG changes. All patients with interictal records of idiopathic generalized seizures had their seizure clusters controlled on different regimens. Three patients with GTCS semiology. First patient was on sodium valproate& levetiracetam. His clusters were controlled on increasing dose of levetiracetam. Second patient was on combination of levetiracetam, sodium valproate, phenobarbitone & clobazam. When dose of sodium valproate was increased his clusters were controlled. Another patient was on combination of valproic acid, levetiracetam, carbamazepine, brivaracetam & clobazam. When dose of carbamazepine was increased his clusters were controlled. The patient with absence semiology who was on monotherapy with drug sodium valproate had his clustered seizures controlled with increase in dose of sodium valproate. Another patient with myoclonic semiology on drug sodium valproate monotherapy, when dose was increased his clustered seizures were controlled. (table 12)

There were five patients with focal epileptiform activity arising from frontal lobe. Two patients had clustered seizures controlled with GTCS semiology. One patient was on combination of sodium valproate, carbamazepine & lamotrigine. His seizures were controlled when the dose of sodium valproate was increased. Another patient was on combination of sodium valproate, ethosuximide & lamotrigine. His

clustered seizures were controlled when dose of lamotrigine was increased. (table 12)

There were three patients of GTCS semiology with focal epileptiform activity arising from right parietotemporal lobe. Out of them, two patients had clustered seizures controlled with different drug combinations. One patient was on combination of carbamazepine, levetiracetam, divalproex & clobazam. When dose of levetiracetam was increased his clustered seizures were controlled. Another patient was on combination of sodium valproate, carbamazepine & levetiracetam. His clustered seizures were controlled when dose of levetiracetam was increased. One patient with occipital seizures had clustered seizures control when dose of oxcarbazepine was increased and brivaracetam was added to drug combination of oxcarbazepine & lamotrigine.(table 12)

Among the patient cohort, 3 patients discussed earlier has both EEG findings and MRI lesion positive (n=3). First patient who had both MTS and interictal records of idiopathic generalized seizures, was on combination of levetiracetam, sodium valproate and clobazam. His clustered seizures were controlled when dose of levetiracetam was increased. Another patient who had cerebral atrophy with focal epileptiform activity arising from frontal lobe was on combination of sodium valproate, carbamazepine, lamotrigine. His clusters were controlled when dose of sodium valproate was increased and clobazam was added to treatment (table 13)

There were only 6 patients on monotherapy. Three patients with GTCS semiology had their clustered seizure controlled with carbamazepine (n=1), levetiracetam (n=1) and oxcarbazepine (n=1). Among these patients, dose of oxcarbazepine was increased. One patient with absence semiology who was on sodium valproate, his clustered seizures were controlled when dose of sodium valproate was increased(table 14)

There were 60 patients on polytherapy. Fourteen patients had sodium valproate as their primary drug with GTCS semiology. Ten of them had their clustered seizures controlled by modification of doses. First patient was on drug combination of sodium valproate and lamotrigine, seizure cluster control was due to increase in the dose of sodium valproate. Second patient had sodium valproate and levetiracetam. His seizures were controlled when dose of levetiracetam was increased. Five patients were on three drugs combinations. First patient had sodium valproate, lamotrigine & ethosuximide, when dose of lamotrigine was increased his clustered seizures were controlled. Second patient had sodium valproate, lacosamide & lorazepam, dose of lacosamide was increased. Third patient had sodium valproate & clobazam, his clustered seizures were controlled when oxcarbazepine was added. Fourth patient had sodium valproate, levetiracetam &lacosamide, dose of levetiracetam was increased. Fifth patient had sodium valproate, lamotrigine& clobazam, dose of sodium valproate was increased and clobazam was decreased. (table 15)

In the sodium valproate group two patients were on 4 drugs combination. First patient had sodium valproate, levetiracetam, carbamazepine, his clustered seizures were controlled when clobazam was added. Second patient was on sodium valproate, phenytoin, levetiracetam, he had his clustered seizures controlled when carbamazepine was added. One patient was on 5 drugs combinations of sodium valproate, brivaracetam, levetiracetam, carbamazepine &clobazam, his clustered seizures were controlled when dose of carbamazepine was increased. (table 15)

Levetiracetam was primary drug in 7 patients of which 5 patients had controlled clustered seizures. They were on different drug regimens. First patient was on levetiracetam & oxcarbazepine when dose of oxcarbazepine was increased his clustered seizures were controlled. Second patient was on levetiracetam, sodium valproate. When sodium valproate was discontinued and phenytoin was added his seizures were controlled. Two patients were on combination of levetiracetam,

carbamazepine and clobazam. Their seizures were controlled when dose of carbamazepine was increased. Another patient on combination of levetiracetam, sodium valproate, phenobarbitone &clobazam, his seizures were controlled when dose of sodium valproate was increased. (table 15)

3 patients with GTCS semiology had controlled clustered seizures with carbamazepine as primary drug. They were on different drug regimens. First patient was on carbamazepine& phenytoin. When primary drug dose was increased his clustered seizures were controlled. Second patient was on combination of carbamazepine, divalproex, levetiracetam & clobazam. He had his clustered seizures controlled when dose of clobazam was increased. Third patient was on combinations of carbamazepine, phenobarbitone, lamotrigine, phenytoin & clobazam. His seizure clusters were controlled when dose of carbamazepine was increased.(table 15)

There were five patients with oxcarbazepine as primary drug. Two patients had their clustered seizures controlled who were on 2 drug and three drugs combinations. First patient had oxcarbazepine &clobazam, when dose of clobazam was decreased his seizures were controlled. Another patient had oxcarbazepine and lamotrigine. His seizure clusters were controlled when brivaracetam was added to it. (table 15)

Three patients had phenytoin as primary drug of which one patient had controlled clustered seizures who was on combination of phenytoin& clobazam, when dose of clobazam was increased.(table 15)

Eighteen Patients were on polytherapy with tonic clonic semiology. Four patients had their primary drug carbamazepine out of which 3 patients had their clustered seizures controlled. They were on drug combinations of carbamazepine, sodium valproate& clobazam. When sodium valproate was discontinued clustered seizures were controlled. Second patient was on carbamazepine, levetiracetam, lacosamide &clobazam, when dose of clobazam was increased and lacosamide

was decreased clustered seizures were controlled. Another patient was on combination of carbamazepine, phenytoin, phenobarbitone. When clobazam was added to this combination and dose of phenobarbitone was increased clustered seizures were controlled. (table 16)

Four patients had levetiracetam as primary drug. Out of which three patients had seizure clusters controlled. First patient was on combination of levetiracetam, carbamazepine &sodium valproate. When dose of sodium valproate was increased clustered seizures were controlled. Second patient was on combination of levetiracetam, phenytoin& clobazam. When dose of primary drug was increased clustered seizures were controlled. Another patient with combination of levetiracetam, sodium valproate, perampanel &clobazam. When dose of clobazam was increased, his clustered seizures were controlled.(table 16)

There were seven patients with oxcarbazepine as primary drug out of which 3 patients had cluster seizures controlled. They were on different drug combinations. First patient was on oxcarbazepine &sodium valproate. Second patient was on oxcarbazepine, brivaracetam &divalproex. When dose of primary drug was increased their clustered seizures were controlled. Third patient was on drug combination of oxcarbazepine, levetiracetam & lacosamide. When the dose of levetiracetam was decreased clustered seizures were controlled. (table 16)

Two patients with sodium valproate as primary drug had their seizure clusters controlled. They were on drug combination of sodium valproate& levetiracetam. When dose of primary drug was increased clustered seizures were controlled. Another patient was on combination of sodium valproate, levetiracetam& clobazam. When dose of levetiracetam was increased clustered seizures were controlled. (table 16)

There were three patients with absence semiology on polytherapy. One patient with primary drug levetiracetam had seizure clusters controlled.

He was on combination of levetiracetam & carbamazepine. When dose of carbamazepine was increased clustered seizures were controlled. (table 17)

There were two patients with myoclonic semiology who had sodium valproate as primary drug. One patient had seizures controlled. He was on drug combinations of sodium valproate, levetiracetam &clobazam, when dose of clobazam was increased clustered seizures were controlled. (table 18)

As there are 178 drugs used in patients of seizure clusters in our study. The most commonly used antiseizure medications in patients with seizure clusters wereclobazam in 34 patients (19.1%) with 2 drug combinations in 4 patients, 3 drug combination in 15 patients, 4 drugs combination in 12 patients and 5 drugs combination in3 patients, followed by levetiracetam n=30(16.9%) with 2 drugs combination in 8 patients, 3 drug combination in 13 patients, 4 drugs combination in 7 patients and 5 drug combination in 2 patients, sodium valproate n=27 (15.2%) 2 drug combination in 7 patients, 3 drug combination in 12 patients, 4 drugs combination in 6 patients and 5 drug combination in 2 patients, carbamazepine n=24(13.5%) 2 drug combination in 4 patients, 3 drugs combination in 9 patients, 4 drug combination in 9 patients and 5 drug combination in 2 patients, oxcarbazepine n=16(9%) with 2 drug combination in 6 patients,3 drugs combination in 8 patients, 4 drug combination in 2 patients, phenytoin n=12(6.7%) with 2 drug combination in 4 patients,3 drugs combination in 4 patients, 4 drug combination in 3 patients and 5 drugs combination in 1 patient, lamotrigine n=8(4.5%) with 2 drug combination in 2 patients,3 drugs combination in 3 patients,4 drugs combination in 2 patients and 5 drug combination in 1 patient, phenobarbitone n=7(3.9%) with 3 drug combination in 1 patient,4 drug combination in 4 patients and 5 drug combination in 2 patients, lacosamide n=6(3.4%) with 3 drug combination in 4 patients and 4 drug combination in 2 patients, brivaracetam n=5(2.8%) with 3 drugs combination in 3 patients, 4 drug combination in 1 patients and 5 drug combination in 1 patient,

topiramate n=4(2.2%) with 3 drugs combination in 3 patients and 4 drugs in 1 patient, divalproex n=2(1.1%) with 3 drug combination in 1 patient and 4 drugs combination in 1 patient, vigabatrin n=1(0.5%) in 5 drugs combination, perampanel n=1(0.5%) in 4 drugs combination and ethosuximide n=1(0.5%) in 3 drugs combination. (figure 12).

Factors which lead to control of seizure clusters in patients on polytherapy were increase in dose of drug in carbamazepine (n=6), sodium valproate (n=5), levetiracetam (n=5), clobazam (n=5), oxcarbazepine (n=4), lamotrigine (n=1), phenobarbitone (n=1) and lacosamide (n=1). Second factor was addition of clobazam in 2 patients, oxcarbazepine (n=1), carbamazepine (n=1), phenytoin (n=1) and brivaracetam (n=1). Third factor was decrease in dose of clobazam in 2 patients, lacosamide in 1 patient and levetiracetam in 1 patient. Fourth factor was discontinuation of sodium valproate in 2 patients.(table 19)

We lost 7 patients on follow up. Among them 2 patients were on monotherapy and 5 patients were on polytherapy. Among polytherapy patients, 2 patients of focal epilepsy had tonic clonic seizures and among patients of generalized epilepsy, 3 patients with GTCS semiology. Out of 2 monotherapy patients, 1 patient had tonic clonic seizures and other patient had absence seizures. (table 20)

Adverse drug reactions (ADR) were reported in 16 subjects. The most common ADR was drowsiness reported in 6 subjects who were prescribed levetiracetam (n=1), clobazam(n=2), sodium valproate(n=1), oxcarbazepine(n=1) and carbamazepine(n=1). Itching was reported in 5 subjects who were prescribed carbamazepine (n=2), oxcarbazepine (n=2) and phenytoin (n=1). Diarrhoea was reported in 2 subjects with sodium valproate and least common ADRs were yellowing of skin, mouth ulcer and anxiety each in 1 subject with the drugs sodium valproate, levetiracetam respectively (figure 13-15)

Causality assessment was done using WHO-UMC scale (table 19). Causality was certain in 1 patient (levetiracetam n=1). 14 patients on

sodium valproate (n=1), levetiracetam (n=1), carbamazepine(n=1) oxcarbazepine (n=1), clobazam (n=2), sodium valproate(n=2), carbamazepine (n=2), oxcarbazepine (n=2), phenytoin (n=1) and levetiracetam (n=1) had possible causality assessment and 1 patient had probable causality who was on drug sodium valproate.(table 21)

DISCUSSION

Seizure clusters largely affects patient's quality of life. There are number of definitions given by different societies and various organizations therefore lot of variations in incidence of cluster seizures has been reported. Total of 184 patients with seizures were enrolled, 101 being prospectively and 83 retrospectively, of which seizure clustering was seen in 73 of them. However, 7 patients were lost to follow up and data of 66 patients was analysed.

Definition of seizure cluster is an important factor in estimating its incidence. According to our study, seizure cluster was defined as when patients self-reported more than three seizures in 24 h in a cohort of patients attending epilepsy clinic at Dayanand Medical College and Hospital, Ludhiana from September 2019 to December 2023. We found that incidence of seizure clustering in our cohort of people with epilepsy was 39.6%. Our findings are similar to the reported incidence of clustered seizure in the literature (13% to 76%) among out-patients [58]. But this incidence is higher than results by Jafa mehvari & colleagues with 902 patients who also defined cluster seizure as patients self-reported with at least 3 seizures in a 24-hour and reported an incidence of 10.4%.[59]

The study by Sillanpää et al. was conducted in 2008, in which patients were followed for 37 years. In this study, cluster seizure was also defined as three or more episodes of seizure in 24 h. Frequency reported of cluster seizure was 22%[60]. In a cohort study by Martinez et al. in 2009, cluster seizures were defined as three times or more focal or generalized seizures during a period of 24 h. The frequency of cluster seizure in 21,000 people with epilepsy was 3% [31]. A study by Bauer et al has defined seizure clusters as increase in occurrence compared to rate expected from individual mean, incidence reported was 57% with retrospective data [61]. Few authors have reported that higher percentage of clustering can be attributed to the fact that antiseizure medications were lowered and discontinued (in few cases)

in the video-EEG unit to increase the chances of capturing/documenting seizures [62] but in our study the data was not enrolled from video EEG unit as it was conducted in cohort of subjects attending epilepsy clinic. Another factor contributing to higher incidence is that our centre is a tertiary care centre and has special epilepsy clinic so we get difficult to treat PWE who have comorbidities and mostly on polytherapy.

Maximum number of patients with seizure clusters in our study falls in the age group of 21-30 years (n=20, 30.3%) followed by 11-20 years (n=17, 25.8%).14 patients reported seizures in the age group of 0-10 years. There were comparatively less patients reported with clusters in age group >30 years (P= 0.08). Our data demonstrated that age was not associated with clusters as a risk factor. Similar findings were reported by other studies as well. A study by Jyoti Upadhyay which included sample size of 200 patients has analysed that 44% of patients were among the age group of 30-40 with lesser patients in younger and older age group [63]. Another study by Getachew et al at Ethiopia reported that out of 265 patients enrolled in a tertiary care hospital, 102(38.5%) were between 21-30 year of age group and n=65 (24.5%) were between age group of 31-40 [64]

In our study, 66 patients were studied, males being 37(56.1%) and females 29 (43.9%). Similar results were observed in study by Birinus a azeala from Nigeria in which 73 adult cases with clusters had male: female ratio of 39:34 [65] Gurumuthy et al reported similar results with males being more affected than females. In another study by Kalyani et al, 65% of enrolled patients were males and 35% were females [66]. Pasha et al conducted an analytical, cross-sectional study at Bangalore Medical College and Research Institute, Bengaluru and he found that out of 200 patients enrolled, 105 of them (52.5%) of them were males and 95 patients (47.5%) were females [67]. 61 males (67.8%) and 29 females (32.2%) were reported in a cross-sectional study, questionnaire based study by Chinnaiyan et al which was conducted at Sri Devaraj University Academy of higher education and Research,

Kolar, Karnataka [68]. This higher reported prevalence of epilepsy in males could be because of the myths associated with epilepsy which make people conceal information regarding epilepsy especially for female patients as it can become a hurdle in their marriage. In addition, we live in male predominant society, so the male family member's health is the first priority in the family and any ailment is promptly reported and treated.

There is heterogeneity of distribution of people with epilepsy in accordance to the area they live in. In our study, most of the patients were from rural areas (65.2%) because of social stigma among society, cultural beliefs, older treatment methods, and a shortage of health care professionals such as neurologists trained in managing epilepsy in the rural area. Besides social issues, the other possible reasons for this observed difference could be due to to lack of good facilities for antenatal/postnatal care, birth injury, malnutrition, systemic and central nervous system (CNS) infections, high rates of trauma in rural settings. We have also observed the same scenario with a greater number of reported seizure clusters from rural areas (n=43, 65.2%) than urban (n=23, 34.8%). Other studies in concordance to our observation are the BURNs study from Bangalore which has reported a nearly twice higher prevalence of epilepsy in rural areas as compared to the urban areas [69]. Similarly, higher rural rates have been reported for incidence of epilepsy also. An annual rate of incidence of 0.42 per 1,000 per year was reported for rural population by Mani et al., as compared to 0.27 per 100,000 per year for urban population by Banerjee et al [70]. Due to better connectivity and availability options of patient outreach programs, patients from rural area were more than urban area who visited us. As our institute is a renowned and prestigious centre, the patient population visiting OPD on daily basis is very large. Epilepsy healthcare requires urgent attention in the rural areas, especially by taking into consideration the higher rates of epilepsy in these regions.

According to our study, it was found that PWE with cluster seizures had negative family history in 42 patients (63.6%). Our results are similar to a study conducted by Kalyani et al who also have reported that majority of patients did not have a positive family history. Out of 60 (100%) patients, 46 (77%) patients did not have family history of epilepsy and rest 14 (23%) patients had a family history of epilepsy (66). In another study conducted by Ranjan et al at IGIMS Patna from January 2017 to February 2018, it has been found that not even single patient out of 154 enrolled had positive family history [71]. Saad et al conducted a prospective observational study at MESCO college of Pharmacy, Telangana and found that family history was present in only 19 (18.26%) out of total 104 patients enrolled [72]. As stated by Saba jafarpur, consanguine parents of people with epilepsy are four times common factor than others for developing clusters. This has not been reported in our study as consanguinity is not a common practice in this part of world. Especially, the risk is more in patients with GTCS in whom if family history of seizure is absent, a higher caution is needed for risk of clustered seizures as observed in our study. However, seizure clusters can occur even in the absence of any risk factor [28]. This low prevalence of family history could be due to social stigma among people with epilepsy because of which patients or their caregivers hide their family history. Based on clinical features, semiology, relevant history & investigations, familial epilepsy was not reported in any of these included subjects. However, pharmacogenomic testing for familial epilepsies was needed for our study subjects but is not easily available and is expensive.

Several studies have been conducted to identify the risk factors for cluster seizures. Physiological factors such as hormonal changes (like menstruation), sleep, and stress were identified as a risk factor for cluster seizure in some other studies [36]. Our study results show that stress is the main contributing risk factor and other risk factors were sleep deprivation, fever, head trauma, menstruation and delayed developmental milestones for development of seizure clusters. Two

patients had catamenial epilepsy out of which seizures in one patient were controlled. She was on combination of sodium valproate, levetiracetam, carbamazepine. Her seizures were controlled when dose of levetiracetam was increased and clobazam was added. A study by Haut et al. was conducted in 2005 to investigate the risk factors for development of cluster seizure. In this cross-sectional study, three or more seizure episodes during 24 h were reported as cluster seizures, (similar to our case definition of cluster seizure) 29% of patients with cluster seizure had extratemporal epilepsy, and head trauma was recognized as the most important risk factor for cluster incidence [33]. In a similar study by Chen et al. in 2017, 4116 people with epilepsy older than 16 years were studied. The results of this study showed that cluster seizure was independently associated with lower age of onset of seizure, symptomatic generalized epilepsy, central nervous system infection [31]. A study by Jafar mehvari reported that education level, less than one year of seizure free periods, seizure frequency, age of onset, number of antiseizure medications used, systemic diseases, prenatal complication, developmental delay, comorbidities, consanguinity and type of MRI lesion were the common risk factors [59]

Cluster seizures are shown to be associated with various semiologies. The most common seizure semiology among our study cohort was GTCS (62%) followed by tonic clonic (27%), absence (6%) and myoclonic seizures (5%). Similarly, in a study which was conducted by Newale et al, it was shown that 80.3% patients were suffering from generalized seizures and 2.3% with absence seizures, which were similar to our study [73]. 78.8% of patients were suffering from GTCS in a prospective study by Saad et al [72] and patients of cluster seizures in our study also belonged to GTCS semiology (n=44) followed by tonic clonic (n=21), myoclonic (n=3) and absence seizures (n=5). Higher population of patients in GTCS semiology could be because of more reporting in this semiology as the symptoms are unlikely to be missed in these patients but in a study Rui Zhong focal epilepsy was the most common epilepsy type reported by 452 (74.6%) patients [74]. In a study

by Jafar mehavri analysis, frequency of seizure clustering is about 10.4%, about 73.11% of the patients have focal epilepsy, 23.65% generalized epilepsy [59].

As a general principle, medication should be started at a low dose to avoid adverse effects and dose is then gradually increased to reach desired dose as per tolerability and recommended dosage. After reaching maximum permitted dose we change the therapy to polytherapy with addition of one drug at a time, then another and so on till seizures are controlled. In our study, we prescribed antiseizure medications to patients, initially by starting on monotherapy and increasing the dose to its maximum tolerated dose. Patients with uncontrolled seizures on monotherapy were started on polytherapy by addition of 2 drugs, 3 drugs upto 6 drugs maximum based on seizure semiology, affordability, patient tolerability with aim to have lower pill burden and looking up for additional beneficial effects and minimum ADRs and affordability.

MRI abnormalities in seizure cluster patients of our study were mesial temporal sclerosis (MTS) (9.5%), calcified granuloma (1.3%), cerebral atrophy (6.8%), gliotic changes (2.7%). In contrast, Mehvari jafar et al conducted a study in 902 patients and reported that 70.74% of patients with cluster seizures had abnormal brain MRI findings. Out of which, 10 patients (12.1%) had MTS and 16 patients (19.51%) had gliosis atrophy [12]. In our study people with epilepsy who had MTS lesion showed varying degree of cluster seizure control. Patients of tonic clonic seizures had 100% control of clustered seizures as compared to the patients with GTCS semiology who had MTS (n=3) with cluster seizure control of 66.6% (p=0.005). 54 patients in our study did not get an MRI. However, in one patient with tonic clonic seizures who had frontal lobe lesion, dose optimization did not result in seizure control.

EEG abnormalities in our study were observed in 15 patients with seizure clusters. There was no improvement seen in patient with focal epilepsy but patients with interictal records of idiopathic generalized

seizures had 100% control in outcome. Patients with frontal lobe lesion had 40 % control of clustered seizures as compared to 66.7% of patients with lesion in right parieto temporal lobe. There was a single patient with occipital seizure. whose cluster seizure were controlled with various combinations of ASMs.

There were 3 patients with mixed lesions in MRI and EEG changes in our study. One patient with generalized tonic clonic seizures had MTS on MRI and interictal records of idiopathic generalized seizures as dose optimization has resulted in cluster control. Second patient with GTCS semiology had cerebral atrophy on MRI and frontal lobe lesion as EEG changes resulted in control of seizures with dose optimization and add on dosage. Third patient with myoclonic seizures who had MTS on MRI and focal epileptiform activity arising from frontal lobe as EEG changes did not have control of clustered seizures despite dose optimization.

In a study by Valentina who followed up patients for atleast one year reported that 1897 patients were started on first line therapy. Among them 988 patients were started on 2nd line (759 patients as add on therapy & 229 switched therapy). Among patients on 2nd line therapy, 485 were shifted to third line treatment (301 patients with add on treatment & 184 switching therapy) and the most prescribed medications were levetiracetam (42.8% of patients), carbamazepine (13.8%), valproic acid (11.0%) among patients started on first-line therapy [75]. The literature review suggests that patients with symptomatic generalized epilepsy were more likely to report seizure clusters as compared with patients of idiopathic generalized epilepsy and focal epilepsy [31]. There were no patients with focal epilepsy on monotherapy, rather all 18 patients of focal epilepsy with tonic clonic semiology were on polytherapy. There was 100% control of cluster seizures among patients with primary drug sodium valproate and other ASMs. In our cohort, we observed when patients were treated with primary drug carbamazepine or levetiracetam along with other ASM

75% of patients had their seizures controlled as compared to 42.8% of patients with oxcarbazepine as primary drug with other ASMs.

Among generalized epilepsy 66.6% of patients on monotherapy with oxcarbazepine or carbamazepine or levetiracetam based on their characteristics had controlled clustered seizures. There were 37 patients with GTCS semiology on polytherapy. 78.5% of patients had shown seizure cluster control with sodium valproate as primary drug. 71.4% of patients with levetiracetam as primary drug had shown control of seizures. 40% of patients with primary drug oxcarbazepine, 37.5 % of patients with primary drug carbamazepine had shown control and 33.3% of patients with primary drug phenytoin had shown clustered seizures control.

50% of patients who had levetiracetam as primary drug with absence semiology had shown control of cluster seizures. Among the patients with myoclonic semiology use of sodium valproate as primary drug had resulted in seizure clusters control in 50% of patients.

According to study by Roop Gursahaani, only five drugs are effective in the treatment of GTCs in the IGEs: sodium valproate, lamotrigine, topiramate, levetiracetam and zonisamide. However, in our study we used sodium valproate, carbamazepine, levetiracetam, oxcarbazepine and phenytoin. Overall, valproate is accepted as the first-line ASM for the idiopathic generalized epilepsies[76-78]. Levetiracetam is the most commonly used alternative to valproate, and has been shown to be effective against myoclonic seizures as well [79]. The combination of lamotrigine and valproate is probably the best documented so far [80].

A randomized, open-label trial compared Lamotrigine to Valproic acid in absence seizure patients [81]. Although approximately equal proportions of the sodium valproate and lamotrigine groups were seizure free at 1 year (68.4% and 52.6%, respectively), the authors noted the delayed effect of the lamotrigine. The patients on monotherapy had better seizure control due to better compliance owing to less pill burden and no drug interactions.

According to the results of our study, it was observed that patients on polytherapy had better outcome as compared to monotherapy because of decreased dose of drugs and therefore reduction in adverse drug reactions and less risk of developing resistance. Our observations are in contrast to studies such as Badwaik et al who has shown in his prospective study that monotherapy was given in 102 patients (69.8%) while polytherapy was given in (30.1%) of people with epilepsy [82]. Earlier in 1990's monotherapy was the ideal treatment in epilepsy because of no drug interactions, lower cost, better compliance and in many cases improved seizure control compared to polytherapy. Earlier choice of drugs were less and now more than 30 drugs are available. As our centre is a tertiary care centre among which patients are mostly with multidrug resistance and difficult to treat epilepsy, so polytherapy was more common. In our cohort, only 6 patients were on monotherapy and appropriate drug selection and dose optimization resulted in cluster control in 66.7% of these patients. Also, the major proportion of our patients were on polytherapy where various interventions in the form of dose optimization (increase or decrease in dose, add on drugs or tapering of drugs) resulted in control of clustered seizures in 51.6% of these patients. Hence, despite polytherapy, dose optimization and appropriate selection of drugs for combination ASM therapies produced better control of seizures and lesser ADRs.

In present era, as more than 50 antiseizure medications are available, it seems fair that dose of ASMs must be optimized to have better drug tolerability and use ASMs in combination for effective control of seizure clusters. This strategy might help in improving compliance driven by treatment efficacy and patient acceptability by having minimal or none adverse effect augmentation in terms of frequency as well as severity. The drawback would be pill burden, cost and risk of drug-drug interactions. The intervention strategies used alone or in combination in our study included dose optimization by increasing dose which was successful in 90.3% of study subjects and reduction in dose which was effective in 12.9% of study subjects; add on appropriate ASM for 19.3%

of subjects and tapering off ineffective or poorly effective drug in 6.4% of these interventions.

The top 6 ASMs used alone or in combination in our cohort in order of frequency were clobazam, levetiracetam, sodium valproate, carbamazepine, oxcarbazepine and phenytoin. The choice of ASMs as monotherapy or polytherapy was based on patient's characteristics like seizure semiology, highest tolerated dose, frequency of administration, cost and physiological state. In our cohort, in 12 patients who had more than 5 seizure clusters in 24 hours, dual intervention were tried in various combinations which resulted in control of seizure clusters in 50% of these patients.

Among our cohort of patients, we had ADRs in 24.2% of our study subjects. The pattern of ADRs included drowsiness (9.1%), itching (7.6%), diarrhoea (3%), anxiety (1.5%), yellowing of skin (1.5%) and mouth ulcer (1.5%). The causality assessment for these ADRs attributed drowsiness to clobazam, sodium valproate, levetiracetam, carbamazepine and oxcarbazepine; itching to carbamazepine, oxcarbazepine and phenytoin; diarrhoea with sodium valproate; mouth ulcers with levetiracetam; anxiety with levetiracetam; yellowing of skin with sodium valproate. Due to these ADRs, we discontinued oxcarbazepine in one of the patients. Other ADRs were managed conservatively and controlled.

There are several limitations in our study. Firstly, this study included retrospective data which is a limitation by its observational nature itself. Secondly, the cohort consisted of PWE who presented in a tertiary epilepsy centre, resulting in sampling bias to include drug resistant epilepsy or difficult to treat epilepsy. The patients maintained a seizure diary to minimize recall bias for documentation of seizure clusters. However, seizure clusters are expected to have been documented properly for GTCS, tonic clonic, absence and myoclonic seizures provided they were witnessed by a bystander. There is a possibility that the frequency of seizures might have had been missed in case the

seizures happened during sleep or when not witnessed by a bystander or in few instances of absence and myoclonic seizures. Another error could have been reported for count of clustered seizures due to a long seizure or inability of untrained observer to differentiate between two closely occurring sequential seizures. Thirdly, despite judicious dose optimization and choice of various ASM combinations, inability to control seizures could be attributed to non-adherence of therapy as we did not verify adherence by doing TDM in all of our study subjects. Fourthly, we had a small sample size due to the unique clinical condition being studied in our population. Despite our best measures, we lost 9.5% of study subjects. This study highlights a fairly common risk of seizure clusters in patients and has been able to demonstrate more than 50% control of seizure clusters by using combination of interventions. However, this needs to be supplemented with TDM for having objective documentation for patient compliance as dose optimization is at times a tipping point where efficacy, patient tolerability and cost needs to be balanced. Polytherapy is not a hindrance but should be used judiciously for appropriate selection of the drug and proactive monitoring for tolerability, drug interactions and adverse drug reactions.

SUMMARY AND CONCLUSION

Seizure clusters are generally referred to as seizures that occur at close intervals with complete recovery between attacks. Seizure cluster in our study were defined as the patients who reported 3 or more than 3 seizures in 24 hours. Seizure cluster has a significant negative impact on the quality of life of patients and it can threaten patients' life if it progresses into status epilepticus. Several risk factor are associated with occurrence of clusters.

This observational study was conducted in the outpatient department of neurology and epilepsy clinic at Dayanand Medical College and Hospital, Ludhiana and included data from September 2019 to December 2023. Patients who fulfilled the inclusion criteria were included in the study. After obtaining the written informed consent, 184 patients were enrolled in the study. 73 patients had clustered seizures and out of them, 7 patients were lost to follow up. Demographic information and information regarding previous as well as present ASMs intake was recorded in the pre structured proforma. Seizure diary proforma was given to all patients in which record of seizure events was maintained. EEG and MRI were the baseline investigations.

The major observations are as under:

- Incidence of cluster seizures was 39.6% in cohort of people with epilepsy
- Most of the patients with clustered seizures belonged to age group of 21-30 years (30.3%) followed by 11-20 years (25.8%). Clustering of seizures did not show any association with the age of patient.
- There was male preponderance (56.1%) in our study cohort.
- Majority of the patients belonged to rural areas (65.2%)
- There was statistically significant association between lack of family history of epilepsy and occurrence of seizure clusters especially in patients with GTCS semiology

- Major risk factors for development of clustered seizures were stress (33.3%), sleep deprivation (25.5%), fever (19.7%), head trauma (13.7%), menstruation (4.0%) and delayed milestones (4.0%). Risk factors were more common in GTCS semiology patients.
- There was statistically significant association (p=0.005) between presence of seizure clusters and lack of abnormal MRI findings in our study subjects.
- 91% of patients were on polytherapy upto 6 different ASMs as compared to monotherapy (9%).
- Clobazam and levetiracetam were the most commonly used antiseizure medications.
- Seizure control was observed in 55% of patients on polytherapy and 66.7% of patients on monotherapy using interventions in the form of drug & dose optimization based on seizure semiology and other patient factors.
- Common adverse drug reactions reported were drowsiness (9.1%), itching (7.6%), diarrhoea (3%), anxiety (1.5%), yellowing of skin (1.5%) and mouth ulcer(1.5%) of patients.

To conclude

Seizure clusters are common in patients with epilepsy and can be associated with adverse outcomes. Incidence of cluster seizures was 39.6% among cohort of people attending epilepsy clinic at our hospital. Out of those, 56.1% of patients had seizure cluster control after drug and dose optimization of ASM based on semiology and other patient factors. ADRs were reported in 24.2% of subjects. Drowsiness (9.1%) was the most common ADR in patients who were on commonly prescribed ASMs such as levetiracetam, clobazam, carbamazepine, sodium valproate and oxcarbazepine.

Drug optimization can help to control seizure clusters with minimum ADR’s despite polytherapy. Treatment of seizure clusters reduces morbidity, cost of treatment, and improves quality of life for patients and their caregivers.

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S.No	Initials	Age(yr)	Age at onset of seizures (years)	gender	residential area	family history	risk factors	semiology	Seizure Cluster if any	Seizures/ day	Duration(seconds)	Seizure in last 24 hr	MRI findings	EEG findings
1	MK	10	8	f	rural	negative	sleep deprivation	GTCS	yes	7	5	4	cerebral atrophy	focal epileptiform activity arising from frontal lobe
-	-	-	-	-	-	-	-	GTCS	yes	7	-	-	-	-
-	-	-	-	-	-	-	-	GTCS	yes	7	-	-	-	-
2	S	13	9	f	rural	negative	stress	absence	yes	5	5	4	normal	focal epileptiform activity arising from frontal lobe
-	-	-	-	-	-	-	-	absence	yes	5	-	-	-	-
3	JS	21	13	m	urban	negative	stress	absence	yes	4	480	2	normal	no record
-	-	-	-	-	-	-	-	absence	yes	4	-	-	-	-
4	N	8	2.5	f	urban	positive	head trauma	GTCS	yes	4	5	3	no record	no record
-	-	-	-	-	-	-	-	GTCS	yes	4	-	-	-	-
5	PK	2	1	f	urban	negative	no	GTCS	no	2	3	1	cerebral atrophy	no record
6	PS	13	7	m	rural	negative	fever	GTCS	yes	6	480	4	normal	no record
-	-	-	-	-	-	-	-	GTCS	yes	6	-	-	-	-
-	-	-	-	-	-	-	-	GTCS	yes	6	-	-	-	-
-	-	-	-	-	-	-	-	GTCS	yes	6	-	-	-	-
-	-	-	-	-	-	-	-	GTCS	yes	6	-	-	-	-
7	AK	19	9	f	rural	negative	sleep deprivation	GTCS	yes	4	300	6	normal	interictal records of idiopathic generalized seizures
-	-	-	-	-	-	-	-	GTCS	yes	4	-	-	-	-
-	-	-	-	-	-	-	-	GTCS	yes	4	-	-	-	-
-	-	-	-	-	-	-	-	GTCS	yes	4	-	-	-	-
-	-	-	-	-	-	-	-	GTCS	yes	4	-	-	-	-
8	KS	34	30	m	urban	positive	no	GTCS	no	2	180	no	cerebral atrophy	normal
9	PK	41	4.5	f	rural	negative	fever	GTCS	yes	17	5	5	normal	normal
-	-	-	-	-	-	-	-	GTCS	yes	17	-	-	-	-
-	-	-	-	-	-	-	-	GTCS	yes	17	-	-	-	-
10	P	21	4	f	urban	negative	no	GTCS	no	3	60	no	cerebral atrophy	no record
-	-	-	-	-	-	-	-	GTCS	no	3	-	-	-	-
11	R	10	8	m	urban	negative	stress	GTCS	yes	4	480	4	no record	no record
-	-	-	-	-	-	-	-	GTCS	yes	4	-	-	-	-
12	HK	24	17	f	rural	negative	head trauma	GTCS	yes	4	480	7	no record	no record
-	-	-	-	-	-	-	-	GTCS	yes	4	-	-	-	-
-	-	-	-	-	-	-	-	GTCS	yes	4	-	-	-	-
-	-	-	-	-	-	-	-	GTCS	yes	4	-	-	-	-
13	SD	22	13	f	rural	negative	sleep deprivation	GTCS	yes	4	5	5	no record	no record
-	-	-	-	-	-	-	-	GTCS	yes	4	-	-	-	-
14	PK	22	16	f	rural	negative	no	GTCS	no	2	10	no	MTS	normal
15	SS	42	26	m	rural	negative	no	GTCS	no	1	2	no	gliotic changes	normal
-	-	-	-	-	-	-	-	GTCS	no	1	-	-	-	-
-	-	-	-	-	-	-	-	GTCS	no	1	-	-	-	-
16	SK	54	25	f	rural	negative	no	GTCS	no	2	2	no	calcified granuloma	normal
-	-	-	-	-	-	-	-	GTCS	no	2	-	-	-	-
17	SH	30	16	m	rural	negative	no	GTCS	no	2	5	no	neurocysticercosis	normal
18	MK	22	16	m	urban	negative	fever	GTCS	no	1	30	no	cerebral atrophy	normal
19	SK	24	16	f	rural	negative	stress	tonic clonic	no	1	120	no	normal	normal
-	-	-	-	-	-	-	-	tonic clonic	no	1	600	-	-	-
-	-	-	-	-	-	-	-	tonic clonic	no	1	-	-	-	-
-	-	-	-	-	-	-	-	tonic clonic	no	1	-	-	-	-
20	HK	29	15	f	rural	negative	no	GTCS	no	2	1800	no	normal	interictal records of idiopathic generalized seizures
-	-	-	-	-	-	-	-	GTCS	no	2	60	-	-	-
-	-	-	-	-	-	-	-	GTCS	no	2	-	-	-	-
-	-	-	-	-	-	-	-	GTCS	no	2	-	-	-	-
-	-	-	-	-	-	-	-	GTCS	no	2	-	-	-	-
21	HG	17	11	m	rural	negative	no	absence	no	1	180	no	normal	normal
-	-	-	-	-	-	-	-	absence	no	1	-	-	-	-
22	DS	10	10	m	rural	negative	delayed milestones	GTCS	yes	4	-	4	no record	normal

S.No	Initials	CNS examination	comorbidity	Seizure frequency	seizure video	S.No of drugs used in patients	Generic name at start of medication	dosage form	route	dose (mg)	frequency (hrly)	daily dose (mg)	start date of drug
1	MK	normal	NAD	daily	yes	1	sodium valproate	tablet	oral	200	12	400	Tuesday, September 27, 2022
-	-	-	-	-	-	2	lamotrigine	tablet	oral	25	24	25	Tuesday, September 27, 2022
-	-	-	-	-	-	3	carbamazepine	tablet	oral	150	12	300	Tuesday, September 27, 2022
2	S	tremors	NAD	daily	no	1	carbamazepine	tablet	oral	400	12	800	Thursday, September 26, 2019
-	-	-	-	-	-	2	levetiracetam	tablet	oral	500	12	1000	Friday, September 27, 2019
3	JS	tremors	NAD	daily	yes	1	levetiracetam	tablet	oral	500	12	1000	Saturday, September 24, 2022
-	-	-	-	-	-	2	oxcarbazepine	tablet	oral	500	12	1000	Sunday, September 25, 2022
4	N	normal	NAD	monthly	no	1	carbamazepine	syrup	oral	200	24	200	Sunday, November 29, 2020
-	-	-	-	-	-	2	sodium valproate	tablet	oral	800	12	1600	Tuesday, October 4, 2022
5	PK	weakness of limbs	NAD	monthly	no	1	oxcarbazepine	syrup	oral	150	24	150	Wednesday, October 5, 2022
6	PS	normal	NAD	monthly	no	1	clobazam	tablet	oral	100	24	100	Friday, February 22, 2019
-	-	-	-	-	-	2	phenobarbitone	tablet	oral	150	24	150	Friday, February 22, 2019
-	-	-	-	-	-	3	lamotrigine	tablet	oral	100	24	100	Sunday, September 18, 2022
-	-	-	-	-	-	4	carbamazepine	tablet	oral	400	12	800	Sunday, September 18, 2022
-	-	-	-	-	-	5	phenytoin	tablet	oral	100	12	200	Saturday, September 10, 2022
7	AK	normal	NAD	monthly	no	1	brivaracetam	tablet	oral	500	12	1000	Tuesday, January 12, 2021
-	-	-	-	-	-	2	valproic acid	tablet	oral	700	12	1400	Tuesday, January 12, 2021
-	-	-	-	-	-	3	clobazam	tablet	oral	10	24	10	Tuesday, January 12, 2021
-	-	-	-	-	-	4	levetiracetam	tablet	oral	500	12	1000	Monday, April 29, 2019
-	-	-	-	-	-	5	carbamazepine	tablet	oral	100	12	200	Monday, April 29, 2019
8	KS	normal	NAD	daily	no	1	phenytoin	tablet	oral	250	12	500	April 10 2021
9	PK	tremors	NAD	daily	no	1	levetiracetam	tablet	oral	250	12	500	Saturday, February 17, 2018
-	-	-	-	-	-	2	phenytoin	tablet	oral	60	24	60	Saturday, February 17, 2018
-	-	-	-	-	-	3	clobazam	tablet	oral	10	24	10	Saturday, February 17, 2018
10	P	normal	NAD	monthly	no	1	carbamazepine	tablet	oral	400	12	800	Sunday, January 1, 2017
-	-	-	-	-	-	2	levetiracetam	tablet	oral	750	12	1500	Saturday, September 17, 2022
11	R	normal	NAD	monthly	no	1	oxcarbazepine	tablet	oral	600	12	1200	Sunday, August 28, 2022
-	-	-	-	-	-	2	clobazam	tablet	oral	15	24	15	Sunday, August 28, 2022
12	HK	tremors	NAD	weekly	no	1	carbamazepine	tablet	oral	600	12	1200	Monday, July 13, 2015
-	-	-	-	-	-	2	brivaracetam	tablet	oral	100	12	200	Monday, July 13, 2015
-	-	-	-	-	-	3	clobazam	tablet	oral	10	12	20	Wednesday, June 1, 2022
-	-	-	-	-	-	4	Perampanel	tablet	oral	12	24	12	Tuesday, July 14, 2015
13	SD	normal	NAD	monthly	no	1	levetiracetam	tablet	oral	750	12	1500	Monday, February 8, 2021
-	-	-	-	-	-	2	clonazepam	tablet	oral	0.25	24	0.25	Friday, September 9, 2022
14	PK	normal	NAD	2/month	no	1	carbamazepine	tablet	oral	200	12	400	Friday, April 22, 2022
15	SS	normal	hypertension	3/month	no	1	oxcarbazepine	tablet	oral	600	12	1200	Friday, August 20, 2021
-	-	-	-	-	-	2	clobazam	tablet	oral	5	12	10	Friday, August 20, 2021
-	-	-	-	-	-	3	levetiracetam	tablet	oral	1000	12	2000	Friday, July 2, 2021
16	SK	normal	hypertension	1-3/month	no	1	levetiracetam	tablet	oral	800	8	2400	Sunday, March 4, 2018
-	-	-	-	-	-	2	carbamazepine	tablet	oral	600	12	1200	Sunday, March 4, 2018
17	SH	normal	NAD	1-3/month	no	1	levetiracetam	tablet	oral	500	12	1000	Tuesday, October 4, 2022
18	MK	normal	NAD	monthly	no	1	levetiracetam	tablet	oral	1000	12	2000	Friday, November 18, 2022
19	SK	normal	NAD	yearly	no	1	levetiracetam	tablet	oral	750	12	1500	Friday, March 20, 2020
-	-	-	-	monthly	-	2	clobazam	tablet	oral	5	12	10	Friday, March 20, 2020
-	-	-	-	-	-	3	oxcarbazepine	tablet	oral	500	12	1000	Friday, March 20, 2020
-	-	-	-	-	-	4	levetiracetam	tablet	oral	1000	12	2000	Wednesday, November 2, 2022
20	HK	normal	hypertension	weekly	no	1	phenytoin	tablet	oral	300	12	600	Friday, January 8, 2021
-	-	-	-	-	-	2	oxcarbazepine	tablet	oral	600	12	1200	Sunday, January 2, 2022
-	-	-	-	-	-	3	sodium valproate	tablet	oral	15	24	15	Sunday, January 2, 2022
-	-	-	-	-	-	4	carbamazepine	tablet	oral	80	24	80	Sunday, January 2, 2022
-	-	-	-	-	-	5	clobazam	tablet	oral	15	24	15	Friday, August 19, 2022
21	HG	normal	NAD	weekly	no	1	carbamazepine	tablet	oral	400	12	800	02-12-2022
-	-	-	-	-	-	2	lacosamide	tablet	oral	2	24	2	02-12-2022
22	DS	normal	NAD	weekly	no	1	sodium valproate	syrup	oral	500	12	1000	Monday, February 3, 2020

S.No	Initials	Date till continuation of drug	Dose after modification on the day of enrollment	follow up 3 months	ADR if any	controlled y/n
1	MK	Tuesday, September 27, 2022	increased to 800	continued same	drowsiness	yes
-	-	Tuesday, September 27, 2022	continued same	continued same	no	
-	-	Tuesday, September 27, 2022	continued same	clobazam 10 mg added	no	
2	S	Tuesday, September 27, 2022	increased to 1200	continued same	no	yes
-	-	Tuesday, September 27, 2022	continued same	continued same	no	
3	JS	Tuesday, September 27, 2022	increased to 1200	continued same	drowsiness	no
-	-	Tuesday, September 27, 2022	continued same	continued same	no	
4	N	Tuesday, October 4, 2022	Increased to 600	lost to follow up	no	lost to follow up
-	-	Thursday, November 24, 2022	continued same	lost to follow up	no	
5	PK	Wednesday, October 5, 2022	Oxcarbazepine increased to 600	carbamazepine added 10mg	no	yes
6	PS	Tuesday, October 11, 2022	continued same	continued same	no	yes
-	-	Tuesday, October 11, 2022	continued same	continued same	no	
-	-	Tuesday, October 11, 2022	continued same	continued same	no	
-	-	Tuesday, October 11, 2022	increased to 1000	Increased to 1200	no	
-	-	Tuesday, October 11, 2022	continued same	continued same	no	
7	AK	Tuesday, October 11, 2022	continued same	continued same	no	yes
-	-	Tuesday, October 11, 2022	continued same	continued same	no	
-	-	Tuesday, October 11, 2022	continued same	continued same	no	
-	-	Tuesday, October 11, 2022	continued same	continued same	no	
-	-	Tuesday, October 11, 2022	increased to 800	continued same	no	
8	KS	Friday, October 14, 2022	increased to 1000	lost to follow up	no	lost to follow up
9	PK	Tuesday, October 18, 2022	continued same	lost to follow up	no	lost to follow up
-	-	Tuesday, October 18, 2022	continued same	lost to follow up	no	
-	-	Tuesday, October 18, 2022	continued same	lost to follow up	no	
10	P	Tuesday, October 18, 2022	increased to 1200	clobazam added 10mg	drowsiness	yes
-	-	Tuesday, October 18, 2022	continued same	continued same	no	
11	R	Tuesday, October 18, 2022	continued same	continued same	no	yes
-	-	Tuesday, October 18, 2022	reduced to 10	continued same	no	
12	HK	Friday, October 28, 2022	continued same	continued same	no	no
-	-	Friday, October 28, 2022	continued same	continued same	no	
-	-	Friday, October 28, 2022	continued same	continued same	no	
-	-	Friday, October 28, 2022	continued same	stopped	no	
13	SD	Friday, November 18, 2022	increased to 2000	continued same	no	no
-	-	Friday, November 18, 2022	continued same	continued same	no	
14	PK	Friday, November 18, 2022	increased to 800	continued same and clobazam added 5	no	yes
15	SS	Friday, November 18, 2022	continued same	continued same	no	yes
-	-	Friday, November 18, 2022	increased to 20	continued same	no	
-	-	Friday, November 18, 2022	continued same	continued same	itching	
16	SK	Friday, November 18, 2022	continued same	continued same	no	yes
-	-	Friday, November 18, 2022	continued same	continued same and clobazam added 5	no	
17	SH	Friday, November 25, 2022	continued same	lost to follow up	no	lost to follow up
18	MK	Friday, November 25, 2022	continued same	decreased to 1500 and carbamazepine added 600	no	yes
19	SK	Friday, December 2, 2022	continued same	continued same	no	yes
-	-	Friday, December 2, 2022	continued same	continued same	drowsiness	
-	-	Friday, December 2, 2022	increased to 1500	continued same	no	
-	-	Friday, December 2, 2022	continued same	continued same	no	
20	HK	Friday, December 2, 2022	continued same	continued same	no	no
-	-	Friday, December 2, 2022	continued same	continued same	drowsiness	
-	-	Friday, December 2, 2022	continued same	continued same	no	
-	-	Friday, December 2, 2022	continued same	continued same	no	
-	-	Friday, December 2, 2022	continued same	continued same	no	
21	HG	Thursday, November 3, 2022	continued same	continued same	no	yes
-	-	Thursday, November 3, 2022	continued same	continued same	no	
22	DS	Friday, December 9, 2022	increased to 1500	lost to follow up	no	lost to follow up

S.No	Initials	Age(yr)	Age at onset of seizures (years)	gender	residential area	family history	risk factors	semiology	Seizure Cluster if any	Seizures/ day	Duration(seconds)	Seizure in last 24 hr	MRI findings	EEG findings
-	-	-	-	-	-	-	-	GTCS	yes	4	5	-	-	-
23	RK	16	9	m	rural	negative	stress	GTCS	yes	4	60	3	no record	focal epileptiform activity arising from frontal lobe
-	-	-	-	-	-	-	-	GTCS	yes	4	5	-	-	-
-	-	-	-	-	-	-	-	GTCS	yes	4	-	-	-	-
-	-	-	-	-	-	-	-	GTCS	yes	4	-	-	-	-
24	GK	25	12	m	urban	negative	no	tonic clonic	no	1	120	no	normal	normal
-	-	-	-	-	-	-	-	tonic clonic	no	1	-	-	-	-
-	-	-	-	-	-	-	-	tonic clonic	no	1	-	-	-	-
-	-	-	-	-	-	-	-	tonic clonic	no	1	-	-	-	-
-	-	-	-	-	-	-	-	tonic clonic	no	1	-	-	-	-
25	MK	29	20	f	rural	negative	no	GTCS	no	1	5	no	west syndrome	interictal records of idiopathic generalized seizures
-	-	-	-	-	-	-	-	GTCS	no	1	-	-	-	-
26	MG	31	11	m	urban	negative	no	GTCS	no	1	60	no	normal	normal
-	-	-	-	-	-	-	-	GTCS	no	1	-	-	-	-
27	KS	15	12	m	rural	negative	sleep deprivation	tonic clonic	yes	5	2	4	MTS	no record
-	-	-	-	-	-	-	-	tonic clonic	yes	5	-	-	-	-
-	-	-	-	-	-	-	-	tonic clonic	yes	5	-	-	-	-
-	-	-	-	-	-	-	-	tonic clonic	yes	5	-	-	-	-
-	-	-	-	-	-	-	-	tonic clonic	yes	5	-	-	-	-
28	EK	29	9	f	rural	negative	stress	tonic clonic	yes	4	480	5	normal	no record
-	-	-	-	-	-	-	-	tonic clonic	yes	4	-	-	-	-
-	-	-	-	-	-	-	-	tonic clonic	yes	4	-	-	-	-
-	-	-	-	-	-	-	-	tonic clonic	yes	4	-	-	-	-
29	AM	3	2.5 months	m	rural	negative	no	GTCS	no	3	480	no	normal	focal epileptiform activity arising from frontal lobe
-	-	-	-	-	-	-	-	GTCS	no	3	-	-	-	-
30	R	25	20	f	rural	negative	head trauma	GTCS	yes	4	60	6	no record	interictal records of idiopathic generalized seizures
-	-	-	-	-	-	-	-	GTCS	yes	4	-	-	-	-
31	AT	39	36	m	rural	negative	fever	GTCS	yes	5	420	5	no record	focal epileptiform activity arising from right parieto temporallobe
-	-	-	-	-	-	-	-	GTCS	yes	5	-	-	-	-
-	-	-	-	-	-	-	-	GTCS	yes	5	480	-	-	-
-	-	-	-	-	-	-	-	GTCS	yes	5	-	-	-	-
32	M	25	12	f	urban	negative	fever	myoclonic	yes	4	320	4	normal	no record
-	-	-	-	-	-	-	-	myoclonic	yes	4	-	-	-	-
-	-	-	-	-	-	-	-	myoclonic	yes	4	360	-	-	-
33	RR	23	15	f	rural	negative	sleep deprivation	GTCS	yes	4	240	no	no record	interictal records of idiopathic generalized seizures
-	-	-	-	-	-	-	-	GTCS	yes	4	-	-	-	-
-	-	-	-	-	-	-	-	GTCS	yes	4	5	-	-	-
-	-	-	-	-	-	-	-	GTCS	yes	4	-	-	-	-
34	SS	39	35	f	-	negative	-	GTCS	no	1	60	2	normal	focal epileptiform activity arising from frontal lobe
35	YS	45	30	m	rural	negative	no	GTCS	no	1	120	2	no record	focal epileptiform activity arising from frontal lobe
36	SS	25	18	m	rural	negative	no	absence	no	1	120	3	normal	focal epileptiform activity arising from frontal lobe
-	-	-	-	-	-	-	-	absence	no	1	-	-	-	-
-	-	-	-	-	-	-	-	absence	no	1	-	-	-	-
37	PK	23	20	f	rural	negative	stress	GTCS	yes	4	180	3	normal	no record
-	-	-	-	-	-	-	-	GTCS	yes	4	-	-	-	-
38	KS	21	15	m	rural	negative	sleep deprivation	GTCS	yes	4	90	4	no record	no record
-	-	-	-	-	-	-	-	GTCS	yes	4	-	-	-	-
-	-	-	-	-	-	-	-	GTCS	yes	4	-	-	-	-
-	-	-	-	-	-	-	-	GTCS	yes	4	-	-	-	-
39	RK	43	20	f	urban	negative	no	GTCS	no	4	420	1	normal	focal epileptiform activity arising from frontal lobe
40	RK	22	20	f	rural	negative	sleep deprivation	GTCS	yes	4	360	3	no record	focal epileptiform activity arising from frontal lobe
-	-	-	-	-	-	-	-	GTCS	yes	4	-	-	-	-
-	-	-	-	-	-	-	-	GTCS	yes	4	-	-	-	-

S.No	Initials	CNS examination	comorbidity	Seizure frequency	seizure video	S.No of drugs used in patients	Generic name at start of medication	dosage form	route	dose (mg)	frequency (hrly)	daily dose (mg)	start date of drug
-	-	-	-	daily	-	2	oxcarbazepine	tablet	oral	600	12	1200	Friday, February 4, 2022
23	RK	normal	NAD	daily	no	1	oxcarbazepine	tablet	oral	600	12	1200	Thursday, March 2, 2017
-	-	-	-	daily	-	2	clobazam	tablet	oral	10	12	20	Friday, March 1, 2019
-	-	-	-	-	-	3	phenobarbitone	tablet	oral	30	12	60	Friday, March 1, 2019
-	-	-	-	-	-	4	lamotrigine	tablet	oral	100	12	200	Friday, October 14, 2016
24	GK	normal	NAD	daily	no	1	phenytoin	tablet	oral	150	12	300	Sunday, March 4, 2007
-	-	-	-	-	-	2	sodium valproate	tablet	oral	250	12	500	Thursday, June 4, 2020
-	-	-	-	-	-	3	lamotrigine	tablet	oral	25	12	50	Friday, April 5, 2019
-	-	-	-	-	-	4	clobazam	tablet	oral	5	12	10	Friday, April 5, 2019
-	-	-	-	-	-	5	phenobarbitone	tablet	oral	30	12	60	Tuesday, July 5, 2016
25	MK	normal	hypertension	weekly	no	1	sodium valproate	tablet	oral	200	12	400	Tuesday, May 3, 2022
-	-	-	-	-	-	2	phenobarbitone	tablet	oral	100	12	200	Monday, September 4, 2017
26	MG	normal	hypertension	weekly	no	1	oxcarbazepine	tablet	oral	400	12	800	Friday, July 1, 2011
-	-	-	-	-	-	2	clobazam	tablet	oral	5	12	10	Friday, July 1, 2011
27	KS	normal	NAD	weekly	no	1	oxcarbazepine	tablet	oral	600	12	1200	Saturday, September 4, 2021
-	-	-	-	-	-	2	clobazam	tablet	oral	5	12	10	Saturday, September 4, 2021
-	-	-	-	-	-	3	lacosamide	tablet	oral	200	12	400	Tuesday, July 6, 2021
-	-	-	-	-	-	4	levetiracetam	tablet	oral	1000	12	2000	Sunday, January 20, 2019
-	-	-	-	-	-	5	carbamazepine	tablet	oral	400	12	800	Wednesday, March 7, 2007
28	EK	normal	hypertension	weekly	no	1	vigabatrin	tablet	oral	500	12	1000	Thursday, February 4, 2021
-	-	-	-	-	-	2	clobazam	tablet	oral	10	12	20	Thursday, February 4, 2021
-	-	-	-	-	-	3	phenobarbitone	tablet	oral	60	12	120	Saturday, April 4, 2020
-	-	-	-	-	-	4	levetiracetam	tablet	oral	100	12	200	Thursday, April 4, 2019
29	AM	normal	NAD	weekly	no	1	oxcarbazepine	tablet	oral	450	12	900	Tuesday, January 3, 2023
-	-	-	-	-	-	2	levetiracetam	tablet	oral	1000	12	2000	Thursday, February 7, 2019
30	R	normal	NAD	weekly	no	1	sodium valproate	tablet	oral	800	12	1600	Friday, March 4, 2022
-	-	-	-	-	-	2	levetiracetam	tablet	oral	250	12	500	Sunday, September 5, 2021
31	AT	normal	hypertension	After 2 months	no	1	carbamazepine	tablet	oral	600	12	1200	Saturday, March 8, 2008
-	-	-	-	-	-	2	levetiracetam	tablet	oral	1000	12	2000	Monday, March 4, 2013
-	-	-	-	-	-	3	clobazam	tablet	oral	10	12	20	Friday, January 6, 2023
-	-	-	-	-	-	4	lacosamide	tablet	oral	100	12	200	Monday, February 3, 2014
32	M	normal	NAD	weekly	no	1	levetiracetam	tablet	oral	1000	12	2000	Friday, September 23, 2022
-	-	-	-	-	-	2	clobazam	tablet	oral	5	12	10	Friday, September 23, 2022
-	-	-	-	weekly	-	3	sodium valproate	tablet	oral	200	12	400	Friday, September 23, 2022
33	RR	normal	NAD	weekly	no	1	sodium valproate	tablet	oral	200	12	400	Wednesday, June 5, 2019
-	-	-	-	-	-	2	phenobarbitone	tablet	oral	60	12	120	Wednesday, August 5, 2020
-	-	-	-	daily	-	3	clobazam	tablet	oral	5	24	5	Saturday, July 3, 2010
-	-	-	-	-	-	4	levetiracetam	tablet	oral	500	12	1000	Sunday, August 2, 2020
34	SS	normal	hypertension	weekly	no	1	levetiracetam	tablet	oral	800	12	1600	Monday, February 3, 2020
35	YS	normal	hypertension	weekly	no	1	levetiracetam	tablet	oral	250	12	500 mg	Monday, January 9, 2023
36	SS	normal	NAD	yearly	no	1	oxcarbazepine	tablet	oral	150	12	300	Thursday, September 8, 2022
-	-	-	-	weekly	-	2	phenytoin	tablet	oral	100	12	200	Thursday, September 8, 2022
-	-	-	-	4 till date	-	3	lacosamide	tablet	oral	100	12	200	Thursday, September 8, 2022
37	PK	normal	NAD	weekly	no	1	valproic acid	tablet	oral	100	12	200	Monday, November 14, 2022
-	-	-	-	-	-	2	lamotrigine	tablet	oral	25	12	50	Saturday, November 12, 2022
38	KS	normal	NAD	weekly	no	1	carbamazepine	tablet	oral	400	12	800	Thursday, February 3, 2022
-	-	-	-	weekly	-	2	levetiracetam	tablet	oral	500	12	1000	Thursday, February 3, 2022
-	-	-	-	-	-	3	phenobarbitone	tablet	oral	30	12	60	Thursday, February 3, 2022
-	-	-	-	-	-	4	carbamazepine	tablet	oral	400	12	800	Monday, July 5, 2021
39	RK	normal	NAD	weekly	no	1	levetiracetam	tablet	oral	750	12	750	Friday, January 20, 2023
40	RK	normal	NAD	weekly	no	1	sodium valproate	tablet	oral	500	12	1000	Friday, February 3, 2017
-	-	-	-	-	-	2	lamotrigine	tablet	oral	100	12	200	Saturday, April 3, 2021
-	-	-	-	monthly	-	3	ethosuximide	tablet	oral	125	8	375	Friday, August 5, 2022

S.No	Initials	Date till continuation of drug	Dose after modification on the day of enrollment	follow up 3 months	ADR if any	controlled y/n
-	-	Friday, December 9, 2022	continued same	lost to follow up	no	lost to follow up
23	RK	Friday, December 9, 2022	continued same	continued same	no	
-	-	Friday, December 9, 2022	reduced to 10	continued same	no	no
-	-	Friday, December 9, 2022	increased to 120	continued same clobazam added 10	no	
-	-	Friday, December 9, 2022	continued same	continued same	no	
24	GK	Friday, December 9, 2022	increased to 600	continued same	no	
-	-	Friday, December 9, 2022	continued same	increased 1000 mg	no	
-	-	Friday, December 9, 2022	increased to 100	continued same	no	yes
-	-	Friday, December 9, 2022	continued same	continued same	no	
-	-	Friday, December 9, 2022	continued same	continued same	no	
25	MK	Friday, December 23, 2022	continued same	increased to 1000	no	yes
-	-	Friday, December 23, 2022	continued same	continued same	no	
26	MG	Tuesday, December 27, 2022	continued same	continued same	no	yes
-	-	Tuesday, December 27, 2022	increased to 20	continued same	no	
27	KS	Tuesday, December 27, 2022	continued same	continued same	itching	
-	-	Tuesday, December 27, 2022	increased to 15	continued same	no	
-	-	Tuesday, December 27, 2022	decreased to 200	stopped	no	yes
-	-	Tuesday, December 27, 2022	continued same	continued same	no	
-	-	Tuesday, December 27, 2022	continued same	continued same	no	
28	EK	Tuesday, December 27, 2022	continued same	sodium valproate 4 ml BD	no	
-	-	Tuesday, December 27, 2022	reduced to 10	continued same	drowsiness	no
-	-	Tuesday, December 27, 2022	continued same	continued same	no	
-	-	Tuesday, December 27, 2022	continued same	continued same	no	
29	AM	Tuesday, January 3, 2023	continued same	continued same	no	yes
-	-	Tuesday, January 3, 2023	decreased to 1000	stopped	no	
30	R	Friday, January 6, 2023	continued same	continued same	no	yes
-	-	Friday, January 6, 2023	increased to 1000	continued same	no	
31	AT	Friday, January 6, 2023	continued same	continued same	no	
-	-	Friday, January 6, 2023	continued same	continued same	no	no
-	-	Sunday, January 8, 2023	continued same	continued same	no	
-	-	Friday, January 6, 2023	increased to 400	continued same	no	
32	M	Friday, January 6, 2023	continued same	continued same	anxiety	
-	-	Friday, January 6, 2023	increased to 20	continued same	no	yes
-	-	Friday, January 6, 2023	continued same	continued same	no	
33	RR	10-01-2023	increased to 1000	continued same	no	
-	-	10-01-2023	continued same	continued same	no	yes
-	-	10-01-2023	continued same	continued same	drowsiness	
-	-	10-01-2023	continued same	continued same	no	
34	SS	Friday, January 13, 2023	continued same	continued same	no	yes
35	YS	Friday, January 13, 2023	continued same	increased to 1000	mouth ulcer	no
36	SS	Friday, January 13, 2023	continued same	continued same clobazam added 10	drowsiness	
-	-	Friday, January 13, 2023	continued same	continued same	no	yes
-	-	Friday, January 13, 2023	continued same	continued same	no	
37	PK	Tuesday, January 17, 2023	increased to 500	continued same	no	yes
-	-	Tuesday, January 17, 2023	continued same	continued same	no	
38	KS	Tuesday, January 17, 2023	continued same	Increased to 1200	no	
-	-	Tuesday, January 17, 2023	continued same	continued same	no	no
-	-	Tuesday, January 17, 2023	continued same	continued same	no	
-	-	Tuesday, January 17, 2023	reduced to 400	stopped	no	
39	RK	Friday, January 20, 2023	continued same	increased to 1000 mg daily and carbamazepine 400 added	no	yes
40	RK	Friday, January 20, 2023	continued same	continued same	diarrhoea	
-	-	Friday, January 20, 2023	increased to 400	continued same	no	yes
-	-	Friday, January 20, 2023	continued same	continued same	no	

S.No	Initials	Age(yr)	Age at onset of seizures (years)	gender	residential area	family history	risk factors	semiology	Seizure Cluster if any	Seizures/ day	Duration(seconds)	Seizure in last 24 hr	MRI findings	EEG findings
41	GK	14	9	f	rural	negative	no	GTCS	no	2	420	1	normal	focal epileptiform activity arising from frontal lobe
-	-	-	-	-	-	-	-	GTCS	no	2	-	-	-	-
-	-	-	-	-	-	-	-	GTCS	no	2	-	-	-	-
42	SS	15	10	m	rural	negative	no	GTCS	no	2	180	1	normal	normal
43	GK	23	14	m	rural	negative	no	tonic clonic	no	1	180	1	normal	focal epileptiform activity arising from frontal lobe
-	-	-	-	-	-	-	-	tonic clonic	no	1	-	-	-	-
-	-	-	-	-	-	-	-	tonic clonic	no	1	-	-	-	-
-	-	-	-	-	-	-	-	tonic clonic	no	1	-	-	-	-
44	A	9	5	m	rural	negative	stress	tonic clonic	yes	4	600	3	MTS	no record
-	-	-	-	-	-	-	-	tonic clonic	yes	4	-	-	-	-
-	-	-	-	-	-	-	-	tonic clonic	yes	4	-	-	-	-
45	J	8	4	f	rural	negative	fever	tonic clonic	yes	4	10	2	normal	focal epileptiform activity arising from frontal lobe
-	-	-	-	-	-	-	-	tonic clonic	yes	4	-	-	-	-
46	RJ	24	14	m	rural	negative	stress	GTCS	yes	5	300	5	no record	focal epileptiform activity arising from right parieto temporallobe
-	-	-	-	-	-	-	-	GTCS	yes	5	-	-	-	-
-	-	-	-	-	-	-	-	GTCS	yes	5	-	-	-	-
-	-	-	-	-	-	-	-	GTCS	yes	5	-	-	-	-
47	R	34	24	m	rural	negative	no	GTCS	no	1	300	1	normal	normal
48	M	35	25	m	rural	negative	no	GTCS	no	3	600	1	normal	focal epileptiform activity arising from frontal lobe
-	-	-	-	-	-	-	-	GTCS	no	3	-	-	-	-
49	N	29	25	f	rural	negative	no	GTCS	no	1	300	1	normal	normal
50	JS	30	20	m	rural	positive	fever	tonic clonic	yes	4	1200	5	normal	no record
-	-	-	-	-	-	-	-	tonic clonic	yes	4	-	-	-	-
-	-	-	-	-	-	-	-	tonic clonic	yes	4	-	-	-	-
-	-	-	-	-	-	-	-	tonic clonic	yes	4	-	-	-	-
51	A	10	5	m	rural	negative	head trauma	GTCS	yes	10	360	6	no record	no record
-	-	-	-	-	-	-	-	GTCS	yes	10	-	-	-	-
-	-	-	-	-	-	-	-	GTCS	yes	10	-	-	-	-
52	GK	17	10	f	urban	positive	stress	absence	yes	5	180	4	normal	interictal records of idiopathic generalized seizures
53	JS	18	10	m	rural	positive	no	myoclonic	yes	5	180	6	normal	interictal records of idiopathic generalized seizures
-	-	-	-	-	-	-	-	myoclonic	yes	5	5	-	-	-
54	S	12	2.5	f	rural	negative	stress	tonic clonic	yes	4	90	5	normal	no record
-	-	-	-	-	-	-	-	tonic clonic	yes	4	-	-	-	-
-	-	-	-	-	-	-	-	tonic clonic	yes	4	-	-	-	-
55	HS	17	14	m	rural	negative	no	tonic clonic	no	2	420	1	normal	focal epileptiform activity arising from frontal lobe
-	-	-	-	-	-	-	-	tonic clonic	no	1	-	-	-	-
56	AS	36	36	m	rural	negative	stress	GTCS	no	1	300	1	normal	focal epileptiform activity arising from frontal lobe
-	-	-	-	-	-	-	-	GTCS	no	1	-	-	-	-
57	VS	22	11	m	rural	positive	head trauma	tonic clonic	yes	4	320	4	MTS	no record
-	-	-	-	-	-	-	-	tonic clonic	yes	4	-	-	-	-
58	PK	38	20	f	urban	negative	stress	tonic clonic	no	2	180	1	normal	focal epileptiform activity arising from frontal lobe
59	GS	25	5	m	urban	negative	delayed milestones	GTCS	no	1	600	1	normal	normal
60	S	35	20	f	urban	negative	delayed milestones	GTCS	no	2	600	1	normal	focal epileptiform activity arising from frontal lobe
-	-	-	-	-	-	-	-	GTCS	no	2	-	-	-	-
61	RK	25	9 months	f	urban	negative	no	GTCS	no	1	90	1	normal	no record
-	-	-	-	-	-	-	-	GTCS	no	1	-	-	-	-
-	-	-	-	-	-	-	-	GTCS	no	1	-	-	-	-
62	NS	11	By birth	m	urban	positive	delayed milestones	tonic clonic	yes	4	300	4	normal	no record
-	-	-	-	-	-	-	-	tonic clonic	yes	4	-	-	-	-
-	-	-	-	-	-	-	-	tonic clonic	yes	4	-	-	-	-
63	SK	27	6th std	f	urban	negative	head trauma	GTCS	yes	5	120	4	normal	normal
64	PT	26	15	m	urban	positive	sleep deprivation	tonic clonic	yes	5	180	3	normal	no record
-	-	-	-	-	-	-	-	tonic clonic	yes	5	-	-	-	-
-	-	-	-	-	-	-	-	tonic clonic	yes	5	-	-	-	-

S.No	Initials	CNS examination	comorbidity	Seizure frequency	seizure video	S.No of drugs used in patients	Generic name at start of medication	dosage form	route	dose (mg)	frequency (hrly)	daily dose (mg)	start date of drug
41	GK	normal	NAD	monthly	no	1	levetiracetam	tablet	oral	1500	12	3000	Friday, January 20, 2023
-	-	-	-	-	-	2	lacosamide	tablet	oral	200	12	400	Friday, January 20, 2023
-	-	-	-	-	-	3	lamotrigine	tablet	oral	25	12	50	Sunday, January 22, 2023
42	SS	normal	NAD	monthly	no	1	levetiracetam	tablet	oral	500	12	1000	Friday, April 5, 2019
43	GK	normal	NAD	weekly	no	1	sodium valproate	tablet	oral	1500	12	3000	Thursday, August 5, 2021
-	-	-	-	-	-	2	topiramate	tablet	oral	100	12	200	Thursday, August 5, 2021
-	-	-	-	monthly	-	3	zonisamide	tablet	oral	100	12	200	Thursday, August 5, 2021
-	-	-	-	-	-	4	lacosamide	tablet	oral	100	12	200	Monday, August 5, 2019
44	A	normal	NAD	weekly	no	1	oxcarbazepine	syrup	oral	400	12	800	Thursday, September 5, 2019
-	-	-	-	-	-	2	brivaracetam	tablet	oral	75	12	150	Saturday, January 7, 2023
-	-	-	-	-	-	3	divalproex	tablet	oral	75	12	75	Monday, September 5, 2022
45	J	normal	NAD	weekly	no	1	carbamazepine	tablet	oral	200	12	400	Friday, January 13, 2023
-	-	-	-	weekly	-	2	levetiracetam	tablet	oral	300	12	600	Friday, January 13, 2023
46	RJ	normal	NAD	weekly	no	1	carbamazepine	tablet	oral	600	12	1200	Wednesday, July 4, 2012
-	-	-	-	-	-	2	divalproex	tablet	oral	250	12	250	Wednesday, July 4, 2012
-	-	-	-	-	-	3	levetiracetam	tablet	oral	750	12	1500	Wednesday, July 4, 2012
-	-	-	-	-	-	4	clobazam	tablet	oral	5	12	10	Wednesday, July 4, 2012
47	R	normal	NAD	monthly	no	1	phenytoin	tablet	oral	250	12	500	Saturday, December 17, 2022
48	M	normal	hyperthyroidism	monthly	no	1	carbamazepine	tablet	oral	400	12	800	Thursday, December 4, 2014
-	-	-	-	-	-	2	oxcarbazepine	tablet	oral	150	12	300	Thursday, October 7, 2010
49	N	normal	NAD	daily	no	1	levetiracetam	tablet	oral	500	12	1000	Wednesday, March 22, 2023
50	JS	normal	NAD	monthly	no	1	levetiracetam	tablet	oral	1000	12	2000	Thursday, February 3, 2022
-	-	-	-	monthly	-	2	Perampanel	tablet	oral	3	12	6	Thursday, May 6, 2010
-	-	-	-	-	-	3	sodium valproate	tablet	oral	200	12	400	Friday, June 7, 2002
-	-	-	-	-	-	4	clobazam	tablet	oral	5	12	10	Thursday, May 6, 2010
51	A	normal	NAD	weekly	no	1	sodium valproate	syrup	oral	300	12	600	Wednesday, May 17, 2023
-	-	-	-	-	-	2	lamotrigine	tablet	oral	100	12	200	Wednesday, May 17, 2023
-	-	-	-	-	-	3	clobazam	tablet	oral	5	12	10	Wednesday, May 17, 2023
52	GK	normal	NAD	monthly	no	1	sodium valproate	tablet	oral	400	12	800	Monday, September 7, 2015
53	JS	normal	NAD	monthly	no	1	sodium valproate	tablet	oral	500	12	1000	Thursday, February 3, 2022
-	-	-	-	daily	-	2	sodium valproate	tablet	oral	200	12	400	Thursday, March 4, 2021
54	S	normal	NAD	daily	no	1	levetiracetam	tablet	oral	500	12	1000	Tuesday, January 31, 2023
-	-	-	-	-	-	2	clobazam	tablet	oral	10	24	10	Tuesday, January 31, 2023
-	-	-	-	daily	-	3	phenytoin	tablet	oral	100	12	200	Tuesday, January 31, 2023
55	HS	normal	NAD	weekly	no	1	levetiracetam	tablet	oral	250	24	250	Friday, February 9, 2018
-	-	-	-	-	-	2	oxcarbazepine	tablet	oral	300	12	600	Thursday, March 30, 2023
56	AS	normal	NAD	monthly	no	1	sodium valproate	tablet	oral	500	12	1000	Saturday, April 4, 2020
-	-	-	-	-	-	2	carbamazepine	tablet	oral	30	12	60	Saturday, April 4, 2020
57	VS	normal	NAD	weekly	no	1	levetiracetam	tablet	oral	750	12	1500	Sunday, May 6, 2018
-	-	-	-	-	-	2	sodium valproate	tablet	oral	500	12	1000	Tuesday, May 5, 2015
58	PK	normal	hyperthyroidism	daily	yes	1	levetiracetam	tablet	oral	500	12	1000	Wednesday, March 4, 2015
59	GS	normal	NAD	1/month	no	1	clobazam	tablet	oral	5	24	5	Monday, June 12, 2023
60	S	normal	hyperthyroidism	monthly	yes	1	carbamazepine	tablet	oral	200	12	400	Friday, April 3, 2015
-	-	-	-	-	-	2	clobazam	tablet	oral	5	12	5	Tuesday, February 7, 2023
61	RK	normal	NAD	weekly	yes	1	sodium valproate	tablet	oral	500	12	1000	Tuesday, May 9, 2023
-	-	-	-	-	-	2	oxcarbazepine	tablet	oral	300	12	600	Tuesday, May 9, 2023
-	-	-	-	-	-	3	levetiracetam	tablet	oral	250	12	500	Tuesday, May 9, 2023
62	NS	normal	NAD	10 days	yes	1	carbamazepine	tablet	oral	100	24	100	Saturday, September 8, 2018
-	-	-	-	-	-	2	levetiracetam	tablet	oral	750	12	1500	Friday, March 7, 2003
-	-	-	-	-	-	3	sodium valproate	tablet	oral	300	12	600	Monday, May 29, 2023
63	SK	normal	NAD	weekly	no	1	brivaracetam	tablet	oral	100	24	100	Thursday, November 3, 2022
64	PT	normal	NAD	daily	yes	1	clobazam	tablet	oral	5	24	5	Tuesday, July 12, 2016
-	-	-	-	-	-	2	levetiracetam	tablet	oral	600	12	1200	Tuesday, July 12, 2016
-	-	-	-	-	-	3	oxcarbazepine	tablet	oral	300	12	600	Tuesday, July 12, 2016

S.No	Initials	Date till continuation of drug	Dose after modification on the day of enrollment	follow up 3 months	ADR if any	controlled y/n
41	GK	24-01-2023	continued same	continued same	no	
-	-	24-01-2023	continued same	continued same	no	no
-	-	24-01-2023	increased to 100	continued same	no	
42	SS	27-01-2023	continued same	lost to follow up	no	lost to follow up
43	GK	Friday, February 10, 2023	continued same	continued same	no	
-	-	Friday, February 10, 2023	increased to 400	continued same	no	yes
-	-	Friday, February 10, 2023	continued same	continued same and clobazam added 10	no	
-	-	Friday, February 10, 2023	continued same	continued same	no	
44	A	Friday, February 10, 2023	increased to 1600	continued same	no	
-	-	Friday, February 10, 2023	continued same	continued same	no	yes
-	-	Friday, February 10, 2023	continued same	continued same	no	
45	J	Friday, February 10, 2023	continued same	Increased to 1200	no	no
-	-	Friday, February 10, 2023	continued same	continued same	no	
46	RJ	Friday, February 17, 2023	continued same	continued same	itching	
-	-	Friday, February 17, 2023	continued same	continued same	no	yes
-	-	Friday, February 17, 2023	continued same	increased 2000	no	
-	-	Friday, February 17, 2023	continued same	continued same	no	
47	R	Friday, February 17, 2023	increased to 1000	lost to follow up	no	lost to follow up
48	M	Friday, March 10, 2023	continued same	Increased to 1200	no	no
-	-	Friday, March 10, 2023	increased to 700	continued same	no	
49	N	Tuesday, May 2, 2023	continued same	continued same	no	lost to follow up
50	JS	Tuesday, May 2, 2023	continued same	continued same	no	
-	-	Tuesday, May 2, 2023	continued same	continued same	no	yes
-	-	Tuesday, May 2, 2023	continued same	continued same	no	
-	-	Tuesday, May 2, 2023	continued same	increased to 20	no	
51	A	Wednesday, May 17, 2023	increased to 1000	continued same	diarrhoea	
-	-	Wednesday, May 17, 2023	continued same	continued same	no	no
-	-	Wednesday, May 17, 2023	continued same	continued same	no	
52	GK	Tuesday, May 23, 2023	increased to 1600	continued same	no	yes
53	JS	Tuesday, May 23, 2023	continued same	increased to 1400	no	no
-	-	Tuesday, May 23, 2023	continued same	continued same	no	
54	S	Tuesday, May 30, 2023	continued same	increased to 2000	no	
-	-	Tuesday, May 30, 2023	continued same	continued same	no	yes
-	-	Tuesday, May 30, 2023	continued same	continued same	no	
55	HS	Tuesday, May 30, 2023	increased to 500	continued same	no	no
-	-	Tuesday, May 30, 2023	increased to 800	continued same	no	
56	AS	Tuesday, June 6, 2023	continued same	continued same	yellowing of skin	no
-	-	Tuesday, June 6, 2023	continued same	continued same	no	
57	VS	Tuesday, June 6, 2023	continued same	continued same	no	yes
-	-	Tuesday, June 6, 2023	increased to 2000	continued same	no	
58	PK	Friday, June 9, 2023	continued same	continued same	no	no
59	GS	Tuesday, June 13, 2023	continued same	lost to follow up	no	lost to follow up
60	S	Tuesday, June 13, 2023	continued same	Increased to 1200	no	no
-	-	Tuesday, June 13, 2023	increased to 10	continued same	no	
61	RK	Tuesday, June 13, 2023	continued same	continued same	no	
-	-	Tuesday, June 13, 2023	continued same	increased to 1200	no	yes
-	-	Tuesday, June 13, 2023	increased to 1000	continued same	no	
62	NS	Tuesday, June 27, 2023	continued same	continued same	no	
-	-	Tuesday, June 27, 2023	continued same	continued same	no	yes
-	-	Tuesday, June 27, 2023	increased to 1000	continued same	no	
63	SK	Tuesday, June 27, 2023	continued same	lost to follow up	no	lost to follow up
64	PT	Friday, April 7, 2023	increased to 10	continued same	no	
-	-	Friday, April 7, 2023	continued same	discontinued	no	
-	-	Friday, April 7, 2023	continued same	continued same	no	no

S.No	Initials	Age(yr)	Age at onset of seizures (years)	gender	residential area	family history	risk factors	semiology	Seizure Cluster if any	Seizures/ day	Duration(seconds)	Seizure in last 24 hr	MRI findings	EEG findings
-	-	-	-	-	-	-	-	tonic clonic	yes	5	-	-	-	-
-	-	-	-	-	-	-	-	tonic clonic	yes	5	-	-	-	-
65	AB	28	20	m	urban	negative	stress	tonic clonic	no	3	10	1	normal	no record
66	MS	20	12	m	rural	negative	delayed milestones	GTCS	no	1	5	1	normal	no record
67	BS	7	4 months	m	urban	negative	delayed milestones	absence	no	2	480	1	normal	no record
-	-	-	-	-	-	-	-	absence	no	2	-	-	-	-
-	-	-	-	-	-	-	-	absence	no	2	-	-	-	-
-	-	-	-	-	-	-	-	absence	no	2	-	-	-	-
-	-	-	-	-	-	-	-	absence	no	2	-	-	-	-
68	AKK	49	25	f	urban	negative	fever	GTCS	yes	4	60	3	MTS	focal epileptiform activity arising from right parieto temporallobe
-	-	-	-	-	-	-	-	GTCS	yes	4	-	-	-	-
-	-	-	-	-	-	-	-	GTCS	yes	4	-	-	-	-
69	K	26	10	m	urban	negative	stress	GTCS	yes	5	5	3	no record	no record
-	-	-	-	-	-	-	-	GTCS	yes	5	-	-	-	-
-	-	-	-	-	-	-	-	GTCS	yes	5	-	-	-	-
-	-	-	-	-	-	-	-	GTCS	yes	5	-	-	-	-
70	BS	24	18	m	urban	negative	sleep deprivation	GTCS	yes	4	600	6	normal	no record
-	-	-	-	-	-	-	-	GTCS	yes	4	-	-	-	-
71	SS	28	22	m	rural	negative	no	absence	no	2	600	1	normal	interictal records of idiopathic generalized seizures
-	-	-	-	-	-	-	-	absence	no	2	-	-	-	-
-	-	-	-	-	-	-	-	absence	no	2	-	-	-	-
-	-	-	-	-	-	-	-	absence	no	2	-	-	-	-
72	NK	24	18	f	urban	negative	fever	GTCS	no	1	480	1	normal	interictal records of idiopathic generalized seizures
-	-	-	-	-	-	-	-	GTCS	no	1	-	-	-	-
-	-	-	-	-	-	-	-	GTCS	no	1	-	-	-	-
73	SM	42	12	f	rural	positive	fever	absence	yes	4	600	4	normal	no record
-	-	-	-	-	-	-	-	absence	yes	4	-	-	-	-
-	-	-	-	-	-	-	-	absence	yes	4	-	-	-	-
74	KK	15	6months	f	rural	negative	no	tonic clonic	no	1	10	1	normal	interictal records of idiopathic generalized seizures
-	-	-	-	-	-	-	-	tonic clonic	no	1	-	-	-	-
75	PS	28	15	m	urban	negative	fever	GTCS	yes	4	60	3	normal	normal
-	-	-	-	-	-	-	-	tonic clonic	yes	4	-	-	-	-
-	-	-	-	-	-	-	-	tonic clonic	yes	4	-	-	-	-
-	-	-	-	-	-	-	-	tonic clonic	yes	4	-	-	-	-
76	EK	43	39	m	rural	negative	fever	myoclonic	yes	6	5	3	MTS	focal epileptiform activity arising from frontal lobe
-	-	-	-	-	-	-	-	myoclonic	yes	6	-	-	-	-
-	-	-	-	-	-	-	-	myoclonic	yes	6	-	-	-	-
-	-	-	-	-	-	-	-	myoclonic	yes	6	-	-	-	-
77	KSS	17	13	m	urban	negative	fever	GTCS	yes	4	240	2	normal	normal
-	-	-	-	-	-	-	-	tonic clonic	yes	4	-	-	-	-
78	HS	22	15	m	urban	negative	fever	GTCS	no	2	300	1	normal	interictal records of idiopathic generalized seizures
-	-	-	-	-	-	-	-	GTCS	no	2	-	-	-	-
-	-	-	-	-	-	-	-	GTCS	no	2	-	-	-	-
-	-	-	-	-	-	-	-	GTCS	no	2	-	-	-	-
79	DK	44	20	f	rural	negative	no	GTCS	no	1	480	1	normal	interictal records of idiopathic generalized seizures
-	-	-	-	-	-	-	-	GTCS	no	1	-	-	-	-
80	MS	8	2	m	rural	positive	fever	tonic clonic	yes	4	480	4	normal	normal
-	-	-	-	-	-	-	-	tonic clonic	yes	4	-	-	-	-
-	-	-	-	-	-	-	-	tonic clonic	yes	4	-	-	-	-
-	-	-	-	-	-	-	-	tonic clonic	yes	4	-	-	-	-
81	D	30	13	f	rural	positive	no	absence	no	2	60	1	normal	normal
82	B	14	5	f	rural	negative	no	tonic clonic	no	2	120	1	normal	interictal records of idiopathic generalized seizures
-	-	-	-	-	-	-	-	tonic clonic	no	2	-	-	-	-
83	S	16	10	m	rural	positive	no	tonic clonic	yes	5	120	3	normal	normal

S.No	Initials	CNS examination	comorbidity	Seizure frequency	seizure video	S.No of drugs used in patients	Generic name at start of medication	dosage form	route	dose (mg)	frequency (hrly)	daily dose (mg)	start date of drug
-	-	-	-	-	-	4	lamotrigine	tablet	oral	100	12	200	Tuesday, July 12, 2016
-	-	-	-	-	-	5	vigabatrin	satchet	oral	5	24	5	Tuesday, July 12, 2016
65	AB	normal	NAD	monthly	yes	1	oxcarbazepine	tablet	oral	750	12	1500	Tuesday, November 1, 2022
66	MS	normal	NAD	weekly	yes	1	phenytoin	tablet	oral	100	24	100	Thursday, August 9, 2012
67	BS	normal	NAD	daily	yes	1	oxcarbazepine	tablet	oral	600	12	1200	Thursday, April 7, 2022
-	-	-	-	-	-	2	phenobarbitone	tablet	oral	50	12	100	Thursday, April 7, 2022
-	-	-	-	-	-	3	sodium valproate	tablet	oral	500	12	1000	Thursday, April 7, 2022
-	-	-	-	-	-	4	clobazam	tablet	oral	60	24	60	Thursday, April 7, 2022
-	-	-	-	-	-	5	phenobarbitone	tablet	oral	100	24	100	Thursday, April 7, 2022
68	AKK	normal	NAD	ily since last mon	yes	1	levetiracetam	tablet	oral	500	12	1000	Monday, August 17, 2020
-	-	-	-	after 7 yrs	-	2	carbamazepine	tablet	oral	400	12	800	Monday, August 17, 2020
-	-	-	-	monthly	-	3	sodium valproate	tablet	oral	600	12	1200	Monday, August 17, 2020
69	K	normal	NAD	weekly	yes	1	sodium valproate	tablet	oral	600	12	1200	Monday, March 4, 2019
-	-	-	-	-	-	2	lorazepam	tablet	oral	2	24	2	Monday, March 4, 2019
-	-	-	-	-	-	3	lacosamide	tablet	oral	100	12	200	Monday, March 4, 2019
-	-	-	-	-	-	4	carbamazepine	tablet	oral	200	12	400	Wednesday, February 3, 2016
70	BS	normal	NAD	monthly	yes	1	clobazam	tablet	oral	10	24	10	Saturday, May 3, 2014
-	-	-	-	-	-	2	phenytoin	tablet	oral	100	12	200	Saturday, May 3, 2014
71	SS	normal	NAD	weekly	yes	1	carbamazepine	tablet	oral	400	12	800	Tuesday, June 2, 2020
-	-	-	-	-	-	2	phenobarbitone	tablet	oral	60	24	60	Tuesday, June 2, 2020
-	-	-	-	daily	-	3	clobazam	tablet	oral	10	24	10	Tuesday, June 2, 2020
-	-	-	-	-	-	4	levetiracetam	tablet	oral	1000	12	2000	Monday, June 3, 2013
72	NK	normal	NAD	weekly	yes	1	levetiracetam	tablet	oral	750	24	750	Thursday, March 5, 2020
-	-	-	-	-	-	2	topiramate	tablet	oral	50	24	50	Thursday, March 5, 2020
-	-	-	-	-	-	3	clobazam	tablet	oral	0.25	24	0.25	Thursday, February 2, 2023
73	SM	normal	yperthyroidisr	weekly	yes	1	carbamazepine	tablet	oral	400	12	800	Friday, September 7, 2018
-	-	-	-	-	-	2	clobazam	tablet	oral	10	12	20	Friday, September 7, 2018
-	-	-	-	monthly	-	3	brivaracetam	tablet	oral	100	12	200	Friday, September 7, 2018
74	KK	normal	NAD	weekly	yes	1	lamotrigine	tablet	oral	100	24	100	Monday, February 4, 2013
-	-	-	-	-	-	2	topiramate	tablet	oral	10	12	20	Monday, February 4, 2013
75	PS	normal	NAD	daily	No	1	oxcarbazepine	tablet	oral	150	12	300	Tuesday, March 21, 2023
-	-	-	-	monthly	-	2	carbamazepine	tablet	oral	30	12	60	Tuesday, March 21, 2023
-	-	-	-	-	-	3	clobazam	tablet	oral	5	12	10	Tuesday, March 21, 2023
-	-	-	-	-	-	4	phenytoin	tablet	oral	100	12	200	Tuesday, March 21, 2023
76	EK	normal	NAD	daily	yes	1	sodium valproate	tablet	oral	200	12	400	Monday, June 7, 2021
-	-	-	-	-	-	2	carbamazepine	tablet	oral	100	12	200	Monday, June 7, 2021
-	-	-	-	-	-	3	clobazam	tablet	oral	10	24	10	Monday, June 7, 2021
-	-	-	-	monthly	-	4	topiramate	tablet	oral	50	24	50	Monday, April 24, 2023
77	KSS	normal	NAD	weekly	no	1	carbamazepine	tablet	oral	12	24	12	Friday, December 30, 2022
-	-	-	-	daily	-	2	levetiracetam	tablet	oral	60	24	60	Friday, December 30, 2022
78	HS	normal	NAD	weekly	yes	1	sodium valproate	tablet	oral	400	12	800	Thursday, August 3, 2017
-	-	-	-	-	-	2	clobazam	tablet	oral	10	12	20	Monday, April 24, 2023
-	-	-	-	-	-	3	oxcarbazepine	tablet	oral	450	12	900	Monday, April 24, 2023
-	-	-	-	daily	-	4	levetiracetam	tablet	oral	750	12	1500	Monday, April 24, 2023
79	DK	normal	yperthyroidisr	weekly	yes	1	levetiracetam	tablet	oral	1000	12	2000	Thursday, May 5, 2022
-	-	-	-	-	-	2	carbamazepine	tablet	oral	5	24	5	Thursday, May 5, 2022
80	MS	normal	NAD	weekly	yes	1	oxcarbazepine	tablet	oral	750	12	1500	Thursday, March 4, 2021
-	-	-	-	daily	-	2	clobazam	tablet	oral	10	12	20	Thursday, March 4, 2021
-	-	-	-	-	-	3	topiramate	tablet	oral	100	12	200	Sunday, July 5, 2015
-	-	-	-	-	-	4	clobazam	tablet	oral	10	12	20	Thursday, March 4, 2021
81	D	normal	NAD	weekly	no	1	levetiracetam	tablet	oral	500	12	1000	Friday, August 3, 2018
82	B	normal	NAD	weekly	yes	1	levetiracetam	tablet	oral	500	12	1000	Tuesday, December 21, 2021
-	-	-	-	-	-	2	clobazam	tablet	oral	10	24	10	Tuesday, December 21, 2021
83	S	normal	NAD	3months	yes	1	oxcarbazepine	tablet	oral	900	12	1800	Tuesday, June 30, 2015

S.No	Initials	Date till continuation of drug	Dose after modification on the day of enrollment	follow up 3 months	ADR if any	controlled y/n
-	-	Friday, April 7, 2023	continued same	continued same	no	
-	-	Friday, April 7, 2023	continued same	discontinued	no	
65	AB	Tuesday, April 11, 2023	continued same	continued same	no	yes
66	MS	Friday, March 10, 2023	continued same	continued same	no	yes
67	BS	Tuesday, March 14, 2023	continued same	continued same	no	
-	-	Tuesday, March 14, 2023	continued same	continued same	no	
-	-	Tuesday, March 14, 2023	continued same	continued same	no	no
-	-	Tuesday, March 14, 2023	continued same	continued same	no	
-	-	Tuesday, March 14, 2023	continued same	continued same	no	
68	AKK	Tuesday, March 21, 2023	increased to 1500	continued same	no	
-	-	Tuesday, March 21, 2023	continued same	continued same and clobazam added 5	no	yes
-	-	Tuesday, March 21, 2023	continued same	continued same	no	
69	K	Friday, March 24, 2023	continued same	continued same	no	
-	-	Friday, March 24, 2023	continued same	continued same	no	
-	-	Friday, March 24, 2023	increased to 400	continued same	no	yes
-	-	Friday, March 24, 2023	continued same	continued same	no	
70	BS	Tuesday, March 28, 2023	continued same	continued same	no	no
-	-	Tuesday, March 28, 2023	increased to 400	continued same	no	
71	SS	Tuesday, March 28, 2023	increased to 1600	continued same	no	
-	-	Tuesday, March 28, 2023	continued same	continued same	no	
-	-	Tuesday, March 28, 2023	increased to 20	continued same	no	yes
-	-	Tuesday, March 28, 2023	continued same	continued same	no	
72	NK	Friday, March 31, 2023	continued same	continued same	no	
-	-	Friday, March 31, 2023	continued same	continued same	no	no
-	-	Friday, March 31, 2023	continued same	continued same	no	
73	SM	Tuesday, April 18, 2023	increased to 1600	continued same	itching	
-	-	Tuesday, April 18, 2023	continued same	continued same	no	no
-	-	Tuesday, April 18, 2023	continued same	continued same	no	
74	KK	Tuesday, April 18, 2023	continued same	continued same	no	yes
-	-	Tuesday, April 18, 2023	continued same	continued same carbamazepine added 400	no	
75	PS	Tuesday, April 18, 2023	continued same	lost to follow up	no	
-	-	Tuesday, April 18, 2023	continued same	lost to follow up	no	
-	-	Tuesday, April 18, 2023	continued same	lost to follow up	no	lost to follow up
-	-	Tuesday, April 18, 2023	continued same	lost to follow up	no	
76	EK	Tuesday, April 25, 2023	increased to 800	continued same	no	
-	-	Tuesday, April 25, 2023	continued same	stopped	no	
-	-	Tuesday, April 25, 2023	continued same	continued same	no	no
-	-	Tuesday, April 25, 2023	continued same	continued same	no	
77	KSS	Tuesday, April 25, 2023	continued same	lost to follow up	no	
-	-	Tuesday, April 25, 2023	continued same	lost to follow up	no	lost to follow up
78	HS	Tuesday, May 9, 2023	increased to 1600	continued same	no	
-	-	Tuesday, May 9, 2023	continued same	continued same	no	
-	-	Tuesday, May 9, 2023	continued same	continued same	no	no
-	-	Tuesday, May 9, 2023	continued same	increased to 2000 mg	no	
79	DK	Tuesday, May 9, 2023	continued same	continued same	no	
-	-	Friday, May 12, 2023	continued same	continued same	no	yes
80	MS	Friday, May 12, 2023	continued same	continued same	itching	
-	-	Friday, May 12, 2023	continued same	continued same	no	
-	-	Friday, May 12, 2023	increased to 400	continued same	no	no
-	-	Friday, May 12, 2023	continued same	continued same	no	
81	D	Tuesday, May 16, 2023	continued same	lost to follow up	no	lost to follow up
82	B	Tuesday, May 16, 2023	continued same	continued same	no	
-	-	Tuesday, May 16, 2023	increased to 15	continued same	no	yes
83	S	Monday, November 13, 2023	continued same	continued same	no	

S.No	Initials	Age(yr)	Age at onset of seizures (years)	gender	residential area	family history	risk factors	semiology	Seizure Cluster if any	Seizures/ day	Duration(seconds)	Seizure in last 24 hr	MRI findings	EEG findings
-	-	-	-	-	-	-	-	tonic clonic	yes	5	-	-	-	-
-	-	-	-	-	-	-	-	tonic clonic	yes	5	-	-	-	-
84	HS	18	14	m	urban	negative	head trauma	GTCS	yes	7	420	2	normal	normal
-	-	-	-	-	-	-	-	GTCS	yes	7	-	-	-	-
-	-	-	-	-	-	-	-	GTCS	yes	7	-	-	-	-
-	-	-	-	-	-	-	-	GTCS	yes	7	-	-	-	-
85	DA	40	25	m	rural	positive	no	tonic clonic	yes	4	5	3	normal	normal
-	-	-	-	-	-	-	-	tonic clonic	yes	4	-	-	-	-
86	SS	18	congenital	m	urban	negative	no	GTCS	no	2	600	1	normal	interictal records of idiopathic generalized seizures
-	-	-	-	-	-	-	-	GTCS	no	2	-	-	-	-
-	-	-	-	-	-	-	-	GTCS	no	2	-	-	-	-
87	C	7	2	m	urban	negative	stress	GTCS	yes	4	5	3	normal	normal
-	-	-	-	-	-	-	-	GTCS	yes	4	-	-	-	-
88	NS	20	10	m	rural	negative	no	absence	no	1	90	1	normal	interictal records of idiopathic generalized seizures
-	-	-	-	-	-	-	-	absence	no	1	-	-	-	-
-	-	-	-	-	-	-	-	absence	no	1	-	-	-	-
89	B	25	20	f	rural	negative	no	tonic clonic	no	3	480	1	normal	interictal records of idiopathic generalized seizures
-	-	-	-	-	-	-	-	tonic clonic	no	3	-	-	-	-
90	RV	13	6	m	urban	negative	sleep deprivation	GTCS	yes	7	600	4	normal	normal
91	MK	32	25	f	rural	positive	no	myoclonic	no	2	240	1	normal	normal
-	-	-	-	-	-	-	-	myoclonic	no	2	-	-	-	-
-	-	-	-	-	-	-	-	myoclonic	no	2	-	-	-	-
92	RS	43	30	m	rural	positive	no	GTCS	yes	4	180	4	normal	normal
93	M	28	16	f	rural	negative	no	tonic clonic	no	2	180	no	normal	interictal records of idiopathic generalized seizures
-	-	-	-	-	-	-	-	tonic clonic	no	2	-	-	-	-
94	SC	35	16	f	rural	positive	no	tonic clonic	yes	9	120	4	normal	normal
-	-	-	-	-	-	-	-	tonic clonic	yes	9	-	-	-	-
-	-	-	-	-	-	-	-	tonic clonic	yes	9	-	-	-	-
95	A	17	15	f	urban	negative	no	GTCS	no	2	60	no	normal	interictal records of idiopathic generalized seizures
96	RS	26	20	m	urban	negative	no	GTCS	no	2	120	no	normal	interictal records of idiopathic generalized seizures
-	-	-	-	-	-	-	-	GTCS	no	2	-	-	-	-
-	-	-	-	-	-	-	-	GTCS	no	2	-	-	-	-
-	-	-	-	-	-	-	-	GTCS	no	2	-	-	-	-
97	A	32	20	f	rural	negative	no	tonic clonic	no	2	600	no	normal	interictal records of idiopathic generalized seizures
-	-	-	-	-	-	-	-	tonic clonic	no	2	-	-	-	-
98	RS	31	20	m	rural	negative	no	tonic clonic	no	2	320	no	normal	interictal records of idiopathic generalized seizures
-	-	-	-	-	-	-	-	tonic clonic	no	2	-	-	-	-
99	RK	34	30	f	rural	negative	fever	GTCS	yes	4	300	4	normal	normal
100	R	35	4	m	rural	negative	no	GTCS	no	3	60	no	normal	normal
-	-	-	-	-	-	-	-	GTCS	no	3	-	-	-	-
101	RK	18	12	f	urban	positive	no	tonic clonic	yes	5	480	6	normal	normal
-	-	-	-	-	-	-	-	tonic clonic	yes	5	-	-	-	-
-	-	-	-	-	-	-	-	tonic clonic	yes	5	-	-	-	-
102	BS	37	30	m	rural	positive	no	GTCS	no	2	600	no	normal	normal
103	GK	39	15	f	urban	positive	no	tonic clonic	yes	6	320	3	normal	normal
-	-	-	-	-	-	-	-	tonic clonic	yes	6	-	-	-	-
-	-	-	-	-	-	-	-	tonic clonic	yes	6	-	-	-	-
104	S	15	10	m	rural	negative	stress	GTCS	yes	5	600	2	MTS	normal
-	-	-	-	-	-	-	-	GTCS	yes	5	-	-	-	-
105	SA	30	8	m	rural	positive	no	GTCS	no	1	120	no	normal	normal
-	-	-	-	-	-	-	-	GTCS	no	1	-	-	-	-
-	-	-	-	-	-	-	-	GTCS	no	1	-	-	-	-
106	P	18	10	f	rural	positive	no	GTCS	no	1	5	no	normal	normal
-	-	-	-	-	-	-	-	GTCS	no	1	-	-	-	-

S.No	Initials	CNS examination	comorbidity	Seizure frequency	seizure video	S.No of drugs used in patients	Generic name at start of medication	dosage form	route	dose (mg)	frequency (hrly)	daily dose (mg)	start date of drug
-	-	-	-	-	-	2	sodium valproate	tablet	oral	200	12	400	Tuesday, June 30, 2015
-	-	-	-	monthly	-	3	topiramate	tablet	oral	25	12	50	Tuesday, June 30, 2015
84	HS	tremors	NAD	weekly	yes	1	phenytoin	tablet	oral	50	12	100	Monday, November 6, 2023
-	-	-	-	-	-	2	phenobarbitone	tablet	oral	50	12	100	Monday, November 6, 2023
-	-	-	-	-	-	3	clobazam	tablet	oral	10	12	20	Monday, November 6, 2023
-	-	-	-	once per month	-	4	oxcarbazepine	tablet	oral	600	12	1200	Monday, November 6, 2023
85	DA	lower limb weakess	hyperthyroidism	monthly	yes	1	oxcarbazepine	tablet	oral	300	12	600	Monday, August 21, 2023
-	-	-	-	-	-	2	sodium valproate	tablet	oral	100	12	200	Monday, August 21, 2023
86	SS	normal	NAD	monthly	yes	1	sodium valproate	tablet	oral	200	12	400	Wednesday, October 11, 2023
-	-	-	-	-	-	2	clobazam	tablet	oral	5	12	10	Wednesday, October 11, 2023
-	-	-	-	-	-	3	levetiracetam	tablet	oral	500	12	1000	Wednesday, October 11, 2023
87	C	normal	NAD	aily before surger	yes	1	phenytoin	syrup	oral	100	12	200	Sunday, April 5, 2015
-	-	-	-	-	-	2	clobazam	tablet	oral	5	12	10	Sunday, April 5, 2015
88	NS	normal	NAD	weekly	yes	1	oxcarbazepine	tablet	oral	750	24	750	Wednesday, July 11, 2018
-	-	-	-	-	-	2	sodium valproate	tablet	oral	400	12	800	Wednesday, July 11, 2018
-	-	-	-	4 times daily	-	3	clobazam	tablet	oral	5	12	10	Saturday, July 13, 2019
89	B	normal	NAD	weekly	yes	1	levetiracetam	tablet	oral	500	12	1000	Friday, August 13, 2021
-	-	-	-	once in 3 months	-	2	clobazam	tablet	oral	5	12	10	Friday, August 13, 2021
90	RV	upper limb weakness	NAD	weekly	yes	1	carbamazepine	tablet	oral	100	12	200	Monday, September 6, 2021
91	MK	normal	NAD	weekly	no	1	sodium valproate	tablet	oral	300	12	600	Friday, April 22, 2022
-	-	-	-	weekly	-	2	perampanel	tablet	oral	4	24	4	Friday, April 22, 2022
-	-	-	-	-	-	3	levetiracetam	tablet	oral	750	12	1500	Friday, April 22, 2022
92	RS	normal	NAD	monthly	NO	1	phenobarbitone	tablet	oral	30	12	60	Thursday, November 7, 2019
93	M	normal	NAD	weekly	yes	1	carbamazepine	tablet	oral	400	12	800	Thursday, March 5, 2015
-	-	-	-	-	-	2	phenytoin	tablet	oral	50	12	100	Thursday, March 5, 2015
94	SC	left side hemiparesis	hyperthyroidism	3 months	yes	1	phenobarbitone	tablet	oral	30	12	60	Tuesday, March 5, 2019
-	-	-	-	-	-	2	carbamazepine	tablet	oral	400	12	800	Tuesday, March 5, 2019
-	-	-	-	2 months	-	3	phenytoin	tablet	oral	50	12	100	Tuesday, March 5, 2019
95	A	left side hemiparesis	NAD	3 months	yes	1	levetiracetam	tablet	oral	750	12	1500	Monday, October 9, 2023
96	RS	left side hemiparesis	NAD	weekly	yes	1	perampanel	tablet	oral	6	12	12	Monday, February 3, 2020
-	-	-	-	-	-	2	oxcarbazepine	tablet	oral	600	12	1200	Tuesday, February 4, 2020
-	-	-	-	-	-	3	oxcarbazepine	tablet	oral	300	12	600	Tuesday, February 4, 2020
-	-	-	-	-	-	4	clobazam	tablet	oral	5	12	10	Sunday, October 1, 2023
97	A	left side hemiparesis	type 2 DM	weekly	yes	1	levetiracetam	tablet	oral	500	12	1000	Monday, February 3, 2020
-	-	-	-	-	-	2	phenobarbitone	tablet	oral	15	12	30	Monday, February 3, 2020
98	RS	left side hemiparesis	type 2 DM	weekly	yes	1	levetiracetam	tablet	oral	750	12	1500	Tuesday, October 4, 2022
-	-	-	-	-	-	2	carbamazepine	tablet	oral	30	12	60	Tuesday, October 4, 2022
99	RK	left side hemiparesis	NAD	ost of conciousnes	yes	1	levetiracetam	tablet	oral	500	12	1000	Tuesday, February 3, 2015
100	R	upper limb weakness	type 2 DM	1/20 days	yes	1	phenytoin	tablet	oral	100	12	200	Friday, February 4, 2022
-	-	-	-	-	-	2	clobazam	tablet	oral	10	24	10	Friday, February 4, 2022
101	RK	lower limb weakess	NAD	weekly	yes	1	carbamazepine	tablet	oral	300	12	600	Sunday, July 12, 2020
-	-	-	-	-	-	2	clobazam	tablet	oral	10	24	10	Tuesday, December 1, 2020
-	-	-	-	max. during night	-	3	sodium valproate	tablet	oral	250	12	500	Tuesday, December 1, 2020
102	BS	normal	NAD	weekly	no	1	sodium valproate	tablet	oral	250	12	500	Tuesday, June 29, 2021
103	GK	normal	type 2 DM	weekly	yes	1	levetiracetam	tablet	oral	750	12	1500	Monday, July 2, 2018
-	-	-	-	-	-	2	oxcarbazepine	tablet	oral	500	12	1000	Monday, July 2, 2018
-	-	-	-	-	-	3	lacosamide	tablet	oral	100	12	200	Monday, July 2, 2018
104	S	normal	NAD	weekly	yes	1	levetiracetam	tablet	oral	500	12	1000	Monday, November 2, 2020
-	-	-	-	-	-	2	oxcarbazepine	tablet	oral	600	12	1200	Monday, November 2, 2020
105	SA	normal	NAD	al 5 episodes till n	no	1	clobazam	tablet	oral	5	12	10	Monday, February 3, 2014
-	-	-	-	-	-	2	phenobarbitone	tablet	oral	15	12	30	Monday, March 3, 2014
-	-	-	-	-	-	3	sodium valproate	tablet	oral	250	12	500	Sunday, January 2, 2005
106	P	normal	NAD	weekly	no	1	levetiracetam	tablet	oral	750	12	1500	Tuesday, February 2, 2021
-	-	-	-	-	-	2	phenytoin	tablet	oral	100	12	200	Monday, April 2, 2012

S.No	Initials	Date till continuation of drug	Dose after modification on the day of enrollment	follow up 3 months	ADR if any	controlled y/n
-	-	Monday, November 13, 2023	increased to 800	continued same	no	no
-	-	Monday, November 13, 2023	continued same	continued same	no	
84	HS	Wednesday, November 15, 2023	continued same	continued same	no	no
-	-	Wednesday, November 15, 2023	increased to 200	continued same	no	
-	-	Wednesday, November 15, 2023	continued same	continued same	no	
-	-	Wednesday, November 15, 2023	continued same	continued same	no	
85	DA	Monday, November 20, 2023	increased to 1200	continued same	no	yes
-	-	Monday, November 20, 2023	continued same	continued same	no	
86	SS	Tuesday, November 21, 2023	continued same	continued same	no	yes
-	-	Tuesday, November 21, 2023	increased to 20	continued same	no	
-	-	Tuesday, November 21, 2023	continued same	continued same	no	
87	C	Tuesday, November 28, 2023	continued same	continued same	no	yes
-	-	Tuesday, November 28, 2023	continued same	increased to 20	no	
88	NS	Tuesday, November 28, 2023	continued same	continued same	no	no
-	-	Tuesday, November 28, 2023	continued same	continued same	no	
-	-	Tuesday, November 28, 2023	continued same	continued same	no	
89	B	Saturday, November 18, 2023	continued same	increased to 2000 mg	no	yes
-	-	Saturday, November 18, 2023	continued same	continued same	no	
90	RV	Friday, December 1, 2023	continued same	continued same	no	yes
91	MK	Wednesday, December 6, 2023	continued same	lost to follow up	no	lost to follow up
-	-	Wednesday, December 6, 2023	continued same	lost to follow up	no	
-	-	Wednesday, December 6, 2023	continued same	lost to follow up	no	
92	RS	Sunday, December 10, 2023	continued same	lost to follow up	no	lost to follow up
93	M	Thursday, October 5, 2023	increased to 1200	continued same	no	yes
-	-	Thursday, October 5, 2023	increased to 200	continued same	no	
94	SC	Saturday, October 7, 2023	increased to 120	continued same	no	yes
-	-	Saturday, October 7, 2023	continued same	continued same and clobazam 10 added	no	
-	-	Saturday, October 7, 2023	continued same	continued same	no	
95	A	Monday, October 9, 2023	continued same	continued same	no	yes
96	RS	Tuesday, October 10, 2023	continued same	continued same	no	yes
-	-	Tuesday, October 10, 2023	increased to 1600	continued same	no	
-	-	Tuesday, October 10, 2023	continued same	continued same	no	
-	-	Tuesday, October 10, 2023	continued same	continued same	no	
97	A	Tuesday, October 10, 2023	continued same	increased to 1000 mg BD	no	yes
-	-	Tuesday, October 10, 2023	continued same	continued same	no	
98	RS	Tuesday, October 31, 2023	continued same	continued same	no	no
-	-	Tuesday, October 31, 2023	continued same	continued same	no	
99	RK	Tuesday, October 31, 2023	increased to 1500	continued same	no	yes
100	R	Friday, October 20, 2023	increased to 600	continued same	no	no
-	-	Friday, October 20, 2023	increaesd to 20	continued same	no	
101	RK	Tuesday, February 2, 2021	increased to 1200	continued same	no	yes
-	-	Tuesday, February 2, 2021	continued same	continued same	no	
-	-	Tuesday, February 2, 2021	continued same	stopped	no	
102	BS	Friday, June 25, 2021	continued same	lost to follow up	no	lost to follow up
103	GK	Friday, February 12, 2021	continued same	dose increased 2000 mg	no	yes
-	-	Friday, February 12, 2021	continued same	continued same	no	
-	-	Friday, February 12, 2021	continued same	continued same	no	
104	S	Wednesday, November 3, 2021	continued same	continued same	no	yes
-	-	Wednesday, November 3, 2021	increaesd to 1600	continued same	drowsiness	
105	SA	Tuesday, December 14, 2021	continued same	continued same	no	lost to follow up
-	-	Tuesday, December 14, 2021	continued same	continued same	no	
-	-	Tuesday, December 14, 2021	increased to 1000	continued same	no	
106	P	Tuesday, November 2, 2021	continued same	lost to follow up	no	lost to follow up
-	-	Tuesday, November 2, 2021	increased to 600	continued same	no	

S.No	Initials	Age(yr)	Age at onset of seizures (years)	gender	residential area	family history	risk factors	semiology	Seizure Cluster if any	Seizures/ day	Duration(seconds)	Seizure in last 24 hr	MRI findings	EEG findings
107	S	25	10	f	rural	positive	no	GTCS	no	2	300	no	normal	normal
-	-	-	-	-	-	-	-	GTCS	no	2	-	-	-	-
108	HS	9	2	m	rural	negative	fever	GTCS	yes	4	600	4	normal	normal
-	-	-	-	-	-	-	-	GTCS	yes	4	-	-	-	-
-	-	-	-	-	-	-	-	GTCS	yes	4	-	-	-	-
109	KS	16	2.5	m	urban	negative	no	GTCS	yes	6	600	3	normal	normal
-	-	-	-	-	-	-	-	GTCS	yes	6	-	-	-	-
-	-	-	-	-	-	-	-	GTCS	yes	6	-	-	-	-
110	MS	24	congenital	m	urban	negative	-	GTCS	no	1	320	no	normal	normal
-	-	-	-	-	-	-	-	GTCS	no	1	-	-	-	-
-	-	-	-	-	-	-	-	GTCS	no	1	-	-	-	-
111	JS	37	19	m	rural	positive	no	GTCS	no	2	120	no	normal	normal
-	-	-	-	-	-	-	-	GTCS	no	2	-	-	-	-
112	MK	34	14	f	rural	positive	no	GTCS	no	2	120	no	normal	normal
113	R	48	20	f	rural	negative	menstruation	GTCS	yes	7	360	4	normal	normal
-	-	-	-	-	-	-	-	GTCS	yes	7	-	-	-	-
114	S	7	4	m	rural	negative	stress	GTCS	yes	6	320	5	normal	normal
-	-	-	-	-	-	-	-	GTCS	yes	6	-	-	-	-
115	PG	28	20	m	rural	negative	no	GTCS	no	2	120	no	normal	normal
-	-	-	-	-	-	-	-	GTCS	no	-	-	-	-	-
116	A	45	13	f	rural	negative	menstruation	GTCS	yes	4	10	4	normal	normal
117	AK	9	5	f	rural	negative	no	GTCS	no	2	60	no	normal	normal
118	S	22	10	m	rural	negative	no	GTCS	no	2	120	no	normal	normal
119	MK	38	5	f	rural	negative	no	GTCS	no	2	120	no	normal	normal
120	SS	9	2	f	rural	positive	no	GTCS	no	2	120	no	normal	normal
121	LK	19	16	f	rural	negative	no	GTCS	no	2	180	no	normal	normal
122	HK	11	5	f	rural	negative	no	GTCS	no	2	300	no	normal	normal
123	JK	29	23	f	rural	positive	no	GTCS	no	2	420	no	normal	normal
124	A	22	congenital	m	rural	negative	no	GTCS	no	2	420	no	normal	normal
-	-	-	-	-	-	-	-	GTCS	no	2	-	-	-	-
-	-	-	-	-	-	-	-	GTCS	no	2	-	-	-	-
125	N	20	15	f	rural	negative	no	tonic clonic	no	1	120	no	normal	normal
126	NS	18	20	m	urban	positive	no	tonic clonic	yes	5	420	6	normal	normal
-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
127	SK	24	17	f	rural	negative	no	GTCS	no	1	120	no	normal	normal
-	-	-	-	-	-	-	-	GTCS	no	2	420	no	normal	normal
128	SK	35	16	f	rural	negative	stress	GTCS	yes	7	180	5	normal	normal
-	-	-	-	-	-	-	-	GTCS	yes	7	-	-	-	-
-	-	-	-	-	-	-	-	GTCS	yes	7	-	-	-	-
129	KJ	28	1.5	m	rural	negative	fever	GTCS	no	2	240	no	normal	normal
-	-	-	-	-	-	-	-	GTCS	no	2	-	-	-	-
-	-	-	-	-	-	-	-	GTCS	no	2	-	-	-	-
130	DS	17	10	m	rural	negative	fever	GTCS	no	3	120	no	normal	interictal records of idiopathic generalized seizures
-	-	-	-	-	-	-	-	GTCS	no	3	-	-	-	-
-	-	-	-	-	-	-	-	GTCS	no	3	-	-	-	-
-	-	-	-	-	-	-	-	GTCS	no	3	-	-	-	-
131	GR	25	16	f	rural	negative	no	GTCS	no	3	300	no	normal	interictal records of idiopathic generalized seizures
-	-	-	-	-	-	-	-	GTCS	no	3	-	-	-	-
132	BK	27	16	f	rural	negative	no	GTCS	no	3	240	no	normal	interictal records of idiopathic generalized seizures
133	P	28	16	m	rural	negative	delayed milestones	GTCS	no	2	240	no	normal	interictal records of idiopathic generalized seizures
134	NS	19	10	m	rural	negative	delayed milestones	GTCS	yes	6	120	4	normal	normal
-	-	-	-	-	-	-	-	GTCS	yes	6	-	-	-	-
135	SR	42	18	f	rural	negative	stress	GTCS	yes	5	120	4	normal	normal
-	-	-	-	-	-	-	-	GTCS	yes	5	-	-	-	-

S.No	Initials	CNS examination	comorbidity	Seizure frequency	seizure video	S.No of drugs used in patients	Generic name at start of medication	dosage form	route	dose (mg)	frequency (hrly)	daily dose (mg)	start date of drug
107	S	normal	NAD	weekly	no	1	carbamazepine	tablet	oral	200	12	400	Monday, January 2, 2017
-	-	-	-	-	-	2	carbamazepine	tablet	oral	200	12	400	Monday, January 2, 2017
108	HS	normal	NAD	weekly	yes	1	carbamazepine	tablet	oral	400	12	800	Sunday, January 6, 2019
-	-	-	-	-	-	2	clobazam	tablet	oral	10	12	20	Tuesday, January 8, 2019
-	-	-	-	-	-	3	topiramate	tablet	oral	5	12	10	Tuesday, January 8, 2019
109	KS	normal	NAD	monthly	yes	1	sodium valproate	tablet	oral	250	12	500	Friday, August 6, 2021
-	-	-	-	-	-	2	clobazam	tablet	oral	5	24	5	Tuesday, September 7, 2021
-	-	-	-	-	-	3	carbamazepine	tablet	oral	600	12	1200	Tuesday, September 7, 2021
110	MS	normal	NAD	weekly	no	1	oxcarbazepine	tablet	oral	600	12	1200	Tuesday, September 3, 2019
-	-	-	-	-	-	2	phenobarbitone	tablet	oral	60	24	60	Sunday, May 5, 2013
-	-	-	-	-	-	3	clobazam	tablet	oral	5	12	10	Monday, August 5, 2013
111	JS	normal	NAD	sporadic	no	1	oxcarbazepine	tablet	oral	450	12	900	Wednesday, September 5, 2018
-	-	-	-	-	-	2	perampanel	tablet	oral	10	12	10	Sunday, September 5, 2021
112	MK	normal	NAD	sporadic	no	1	levetiracetam	tablet	oral	750	12	1500	Sunday, August 7, 2011
113	R	normal	type 2 DM	daily	no	1	levetiracetam	tablet	oral	500	12	1000	Friday, August 6, 2021
-	-	-	-	-	-	2	sodium valproate	tablet	oral	150	12	300	Thursday, August 6, 2020
114	S	normal	NAD	weekly	no	1	lamotrigine	tablet	oral	25	12	50	Tuesday, April 20, 2021
-	-	-	-	weekly	-	2	oxcarbazepine	tablet	oral	500	12	1000	Tuesday, April 20, 2021
115	PG	normal	NAD	weekly	no	1	levetiracetam	tablet	oral	750	12	1500	Thursday, September 7, 2017
-	-	-	-	-	-	2	oxcarbazepine	tablet	oral	500	12	1000	Thursday, September 7, 2017
116	A	normal	type 2 DM	monthly	no	1	lamotrigine	tablet	oral	100	12	200	Saturday, August 8, 2020
117	AK	normal	NAD	weekly	no	1	levetiracetam	tablet	oral	750	12	1500	Thursday, May 6, 2021
118	S	normal	NAD	weekly	no	1	levetiracetam	tablet	oral	750	12	1500	Wednesday, March 25, 2020
119	MK	normal	type 2 DM	weekly	no	1	levetiracetam	tablet	oral	750	12	1500	Friday, January 10, 2020
120	SS	normal	NAD	daily	no	1	levetiracetam	tablet	oral	1000	12	2000	Wednesday, February 5, 2020
121	LK	normal	NAD	sporadic	no	1	phenytoin	tablet	oral	250	12	500	Sunday, May 10, 2020
122	HK	normal	NAD	weekly	no	1	phenytoin	tablet	oral	250	12	500	Sunday, May 10, 2020
123	JK	normal	NAD	sporadic	no	1	oxcarbazepine	tablet	oral	150	12	300	Tuesday, May 12, 2020
124	A	normal	NAD	daily	no	1	sodium valproate	tablet	oral	150	12	300	21 Feburary 2019
-	-	-	-	-	-	2	lamotrigine	tablet	oral	100	12	200	21 Feburary 2019
-	-	-	-	-	-	3	clobazam	tablet	oral	10	12	20	21 Feburary 2019
125	N	normal	NAD	weekly	no	1	carbamazepine	tablet	oral	200	12	400	Tuesday, January 19, 2021
126	NS	normal	NAD	daily	no	1	clobazam	tablet	oral	10	12	20	Friday, January 15, 2021
-	-	-	-	-	-	2	levetiracetam	tablet	oral	1000	12	2000	Friday, January 15, 2021
127	SK	normal	NAD	weekly	no	1	carbamazepine	tablet	oral	200	12	400	Tuesday, July 7, 2020
-	-	normal	NAD	weekly	no	2	sodium valproate	tablet	oral	500	12	1000	Monday, February 10, 2020
128	SK	lower limb weakess	type 2 DM	sporadic	no	1	carbamazepine	tablet	oral	200	12	400	Tuesday, February 6, 2018
-	-	-	-	-	-	2	levetiracetam	tablet	oral	750	12	1500	Sunday, September 7, 2014
-	-	-	-	-	-	3	clobazam	tablet	oral	5	12	10	Tuesday, February 7, 2012
129	KJ	right hemipaeresis	NAD	sporadic	no	1	oxcarbazepine	tablet	oral	150	12	300	Friday, June 25, 2021
-	-	-	-	-	-	2	clobazam	tablet	oral	5	12	10	Wednesday, July 7, 2021
-	-	-	-	-	-	3	sodium valproate	tablet	oral	250	12	500	Thursday, June 17, 2021
130	DS	normal	NAD	weekly	no	1	phenytoin	tablet	oral	250	12	500	Tuesday, January 5, 2021
-	-	-	-	-	-	2	phenobarbitone	tablet	oral	60	12	120	Tuesday, January 5, 2021
-	-	-	-	-	-	3	levetiracetam	tablet	oral	75	12	150	Tuesday, January 5, 2021
-	-	-	-	-	-	4	clobazam	tablet	oral	10	12	20	Tuesday, January 5, 2021
131	GR	normal	NAD	weekly	no	1	phenytoin	tablet	oral	100	12	200	Wednesday, February 4, 2015
-	-	-	-	sporadic	-	2	carbamazepine	tablet	oral	200	12	400	Friday, March 6, 2020
132	BK	normal	NAD	monthly	no	1	levetiracetam	tablet	oral	500	12	1000	Tuesday, March 17, 2020
133	P	normal	NAD	daily	no	1	sodium valproate	tablet	oral	500	12	1000	Monday, February 3, 2020
134	NS	normal	NAD	sporadic	no	1	phenytoin	tablet	oral	100	12	200	Friday, May 7, 2010
-	-	-	-	-	-	2	levetiracetam	tablet	oral	500	12	1000	Tuesday, March 3, 2020
135	SR	normal	type 2 DM	weekly	no	1	phenytoin	tablet	oral	100	12	200	Thursday, May 6, 2010
-	-	-	-	-	-	2	sodium valproate	tablet	oral	250	12	500	Friday, April 6, 2018

S.No	Initials	Date till continuation of drug	Dose after modification on the day of enrollment	follow up 3 months	ADR if any	controlled y/n
107	S	Friday, October 29, 2021	increased to 800	lost to follow up	no	lost to follow up
-	-	Friday, October 29, 2021	continued same	continued same	no	
108	HS	Friday, September 24, 2021	continued same	continued same	no	no
-	-	Friday, September 24, 2021	continued same	clobazam added 10	no	
-	-	Friday, September 24, 2021	continued same	continued same	no	
109	KS	Wednesday, September 8, 2021	increased to 1000	continued same	no	no
-	-	Wednesday, September 8, 2021	increased to 10	continued same	no	
-	-	Wednesday, September 8, 2021	continued same	continued same	drowsiness	
110	MS	Tuesday, November 30, 2021	increased to 1600	continued same	no	yes
-	-	Tuesday, November 30, 2021	continued same	continued same	no	
-	-	Tuesday, November 30, 2021	continued same	increased to 20	no	
111	JS	Tuesday, December 7, 2021	continued same	continued same	no	lost to follow up
-	-	Tuesday, December 7, 2021	continued same	continued same	no	lost to follow up
112	MK	Tuesday, August 10, 2021	continued same	lost to follow up	no	lost to follow up
113	R	Monday, May 16, 2022	continued same	continued same	no	yes
-	-	Friday, August 6, 2021	continued same	stopped & phentyoin added 200mg	no	
114	S	Wednesday, September 8, 2021	continued same	continued same	no	yes
-	-	Wednesday, September 8, 2021	increased to 1600	brivaracetam 50 HS added	no	
115	PG	Friday, April 16, 2021	continued same	continued same	no	yes
-	-	Friday, April 16, 2021	continued same	continued same	no	
116	A	Friday, May 21, 2021	increased to 800	dose increased to 1600 mg BD , sodium valproate was added 500	no	no
117	AK	Sunday, June 27, 2021	continued same	continued same	no	yes
118	S	Sunday, June 27, 2021	continued same	continued same	no	no
119	MK	Sunday, June 27, 2021	continued same	continued same	no	no
120	SS	Sunday, June 27, 2021	continued same	continued same	no	lost to follow up
121	LK	Sunday, June 27, 2021	continued same	lost to follow up	no	no
122	HK	Sunday, June 27, 2021	continued same	continued same	no	no
123	JK	Tuesday, May 12, 2020	increased to 600	continued same	no	lost to follow up
124	A	Sunday, March 21, 2021	continued same	continued same	no	yes
-	-	Sunday, March 21, 2021	continued same	continued same	no	
-	-	Sunday, March 21, 2021	continued same	continued same	no	
125	N	Saturday, March 6, 2021	continued same	continued same	no	yes
126	NS	Sunday, July 4, 2021	continued same	continued same	no	no
-	-	Sunday, July 4, 2021	continued same	continued same and carbamazepine 600 added	no	
127	SK	Tuesday, January 19, 2021	continued same	continued same	no	no
-	-	Tuesday, January 19, 2021	continued same	decreased to 600	no	no
128	SK	Tuesday, December 22, 2020	increased to 800	continued same	no	yes
-	-	Tuesday, December 22, 2020	continued same	continued same	no	
-	-	Tuesday, December 22, 2020	continued same	continued same	no	
129	KJ	Saturday, July 17, 2021	increased to 600	continued same	no	no
-	-	Saturday, July 17, 2021	continued same	continued same	no	
-	-	Saturday, July 17, 2021	continued same	continued same	no	
130	DS	Friday, July 2, 2021	continued same	increased to 1000	no	no
-	-	Friday, July 2, 2021	continued same	continued same	no	
-	-	Friday, July 2, 2021	continued same	continued same	no	
-	-	Friday, July 2, 2021	continued same	continued same	no	
131	GR	Friday, March 6, 2020	increased to 600	continued same	no	yes
-	-	Sunday, May 3, 2020	continued same	continued same	no	
132	BK	Tuesday, March 17, 2020	continued same	continued same	no	yes
133	P	Tuesday, March 3, 2020	continued same	stopped & Carbamazepine added 5 mg	no	no
134	NS	Tuesday, March 3, 2020	continued same	continued same	no	no
-	-	Friday, March 6, 2020	continued same	clobazam added 10	no	
135	SR	Tuesday, March 3, 2020	continued same	increased to 600	no	no
-	-	Tuesday, March 3, 2020	continued same	continued same	no	

S.No	Initials	Age(yr)	Age at onset of seizures (years)	gender	residential area	family history	risk factors	semiology	Seizure Cluster if any	Seizures/ day	Duration(seconds)	Seizure in last 24 hr	MRI findings	EEG findings
136	AK	9	3	m	rural	negative	no	GTCS	yes	4	5	3	normal	normal
-	-	-	-	-	-	-	-	GTCS	yes	4	-	-	-	-
137	IK	29	20	f	urban	negative	no	GTCS	no	1	10	no	normal	no record
138	RK	10	5	m	rural	negative	stress	GTCS	yes	4	20	4	MTS	normal
-	-	-	-	-	-	-	-	GTCS	yes	4	-	-	-	-
-	-	-	-	-	-	-	-	GTCS	yes	4	-	-	-	-
139	P	25	20	m	rural	negative	no	GTCS	no	2	300	no	normal	no record
140	BK	43	11	f	rural	negative	no	GTCS	no	3	320	no	normal	no record
141	HM	10	8	m	rural	positive	fever	GTCS	yes	4	180	4	normal	normal
142	N	40	13	f	rural	negative	fever	GTCS	no	2	420	no	normal	normal
143	K	30	22	m	rural	negative	no	GTCS	no	2	600	no	normal	no record
-	-	-	-	-	-	-	-	GTCS	no	2	-	-	-	-
144	A	20	10	f	rural	positive	delayed milestones	GTCS	no	2	420	no	normal	normal
-	-	-	-	-	-	-	-	GTCS	no	2	-	-	-	-
145	MK	29	25	f	rural	positive	sleep deprivation	GTCS	yes	5	600	5	normal	normal
146	AG	54	23	f	rural	positive	no	GTCS	yes	5	180	4	normal	normal
-	-	-	-	-	-	-	-	GTCS	yes	5	-	-	-	-
147	LK	31	23	f	rural	negative	delayed milestones	tonic clonic	no	1	120	no	normal	no record
148	SK	17	12	m	urban	negative	no	GTCS	no	1	120	no	normal	no record
149	AS	24	18	m	urban	positive	fever	tonic clonic	yes	4	120	4	normal	normal
-	-	-	-	-	-	-	-	tonic clonic	yes	4	-	-	-	-
-	-	-	-	-	-	-	-	tonic clonic	yes	4	-	-	-	-
150	BK	34	7	f	urban	negative	no	tonic clonic	no	1	180	no	normal	no record
151	SS	12	6 days	m	rural	negative	fever	GTCS	no	2	180	no	normal	no record
-	-	-	-	-	-	-	-	GTCS	no	2	-	-	-	-
152	GK	34	congenital	f	urban	positive	no	GTCS	yes	5	180	5	calcified granuloma	normal
-	-	-	-	-	-	-	-	GTCS	yes	5	-	-	-	-
153	SS	33	32	m	urban	negative	no	GTCS	no	2	420	no	normal	no record
154	HK	24	17	f	urban	negative	no	GTCS	no	1	240	no	normal	no record
155	SK	36	33	f	urban	positive	no	GTCS	yes	5	420	5	normal	normal
-	-	-	-	-	-	-	-	GTCS	yes	5	300	-	-	-
156	N	33	13	f	urban	negative	no	GTCS	no	1	120	no	normal	no record
-	-	-	-	-	-	-	-	GTCS	no	1	-	-	-	-
157	AS	24	10	m	rural	negative	no	GTCS	no	1	420	no	normal	no record
-	-	-	-	-	-	-	-	GTCS	no	1	-	-	-	-
158	NK	22	9	f	urban	negative	no	GTCS	no	2	180	no	normal	no record
-	-	-	-	-	-	-	-	GTCS	no	2	-	-	-	-
159	MS	28	25	m	urban	positive	sleep deprivation	tonic clonic	yes	5	60	4	normal	normal
-	-	-	-	-	-	-	-	tonic clonic	yes	5	-	-	-	-
-	-	-	-	-	-	-	-	tonic clonic	yes	5	-	-	-	-
160	NS	6	1	m	urban	negative	no	tonic clonic	no	2	120	no	normal	no record
-	-	-	-	-	-	-	-	tonic clonic	no	2	-	-	-	-
-	-	-	-	-	-	-	-	tonic clonic	no	2	-	-	-	-
161	HK	31	23	f	urban	negative	no	GTCS	no	1	10	no	normal	no record
-	-	-	-	-	-	-	-	GTCS	no	1	-	-	-	-
-	-	-	-	-	-	-	-	GTCS	no	1	-	-	-	-
162	AS	18	21	m	rural	negative	no	GTCS	no	2	120	no	normal	no record
-	-	-	-	-	-	-	-	GTCS	no	2	-	-	-	-
-	-	-	-	-	-	-	-	GTCS	no	2	-	-	-	-
163	SK	9	3	f	urban	positive	sleep deprivation	GTCS	yes	4	60	3	normal	normal
-	-	-	-	-	-	-	-	GTCS	yes	4	-	-	-	-
-	-	-	-	-	-	-	-	GTCS	yes	4	-	-	-	-
164	P	25	20	f	rural	positive	no	GTCS	no	2	240	no	normal	normal
-	-	-	-	-	-	-	-	GTCS	no	2	-	-	-	-

S.No	Initials	CNS examination	comorbidity	Seizure frequency	seizure video	S.No of drugs used in patients	Generic name at start of medication	dosage form	route	dose (mg)	frequency (hrly)	daily dose (mg)	start date of drug
136	AK	normal	NAD	sporadic	no	1	carbamazepine	syrup	oral	400	12	800	Friday, February 7, 2020
-	-	-	-	weekly	-	2	phenytoin	tablet	oral	100	12	200	Friday, February 7, 2020
137	IK	normal	type 2 DM	daily	no	1	carbamazepine	tablet	oral	100	12	200	Saturday, August 6, 2016
138	RK	upper limb weakness	NAD	sporadic	no	1	phenytoin	tablet	oral	100	12	200	Thursday, July 5, 2018
-	-	-	-	-	-	2	levetiracetam	tablet	oral	500	12	1000	Thursday, July 5, 2018
-	-	-	-	-	-	3	sodium valproate	tablet	oral	500	12	1000	Friday, February 14, 2020
139	P	upper limb weakness	NAD	weekly	no	1	phenytoin	tablet	oral	100	12	200	Monday, March 25, 2019
140	BK	lower limb weakess	NAD	monthly	no	1	carbamazepine	tablet	oral	400	12	800	Monday, March 2, 2020
141	HM	lower limb weakess	NAD	twice/month	no	1	carbamazepine	syrup	oral	300	12	600	Wednesday, July 4, 2018
142	N	normal	NAD	sporadic	no	1	sodium valproate	tablet	oral	400	12	800	Friday, May 3, 2019
143	K	normal	NAD	sporadic	no	1	carbamazepine	tablet	oral	400	12	800	Friday, March 1, 2019
-	-	-	-	monthly	-	2	phenobarbitone	tablet	oral	30	12	60	Friday, March 1, 2019
144	A	normal	NAD	daily	no	1	phenytoin	tablet	oral	50	12	100	Friday, November 1, 2019
-	-	-	-	sporadic	-	2	phenobarbitone	tablet	oral	30	24	30	Friday, November 1, 2019
145	MK	tremors	type 2 DM	daily	no	1	oxcarbazepine	tablet	oral	450	12	900	Tuesday, April 2, 2019
146	AG	tremors	hyperthyroidisn	weekly	no	1	oxcarbazepine	tablet	oral	300	12	600	Sunday, January 23, 2011
-	-	-	-	-	-	2	clobazam	tablet	oral	5	12	10	Sunday, January 23, 2011
147	LK	tremors	hypertension	daily	no	1	carbamazepine	tablet	oral	200	12	400	Saturday, March 3, 2012
148	SK	tremors	NAD	weekly	no	1	carbamazepine	tablet	oral	300	12	600	Wednesday, August 19, 2020
149	AS	tremors	NAD	monthly	no	1	phenytoin	tablet	oral	150	12	300	Tuesday, May 5, 2015
-	-	-	-	-	-	2	lacosamide	tablet	oral	100	12	200	Tuesday, May 5, 2015
-	-	-	-	-	-	3	oxcarbazepine	tablet	oral	600	12	1200	Wednesday, May 6, 2015
150	BK	tremors	NAD	sporadic	no	1	carbamazepine	tablet	oral	200	12	400	Saturday, June 4, 2016
151	SS	tremors	NAD	daily	no	1	oxcarbazepine	tablet	oral	600	12	1200	Monday, April 1, 2019
-	-	-	-	-	-	2	clobazam	tablet	oral	5	12	10	Monday, April 1, 2019
152	GK	normal	NAD	yearly	no	1	oxcarbazepine	tablet	oral	600	12	1200	Friday, August 14, 2020
-	-	-	-	-	-	2	sodium valproate	tablet	oral	200	12	400	Thursday, October 18, 2018
153	SS	normal	hyperthyroidisn	weekly	no	1	phenobarbitone	tablet	oral	15	12	30	Saturday, July 9, 2016
154	HK	normal	NAD	daily	no	1	oxcarbazepine	tablet	oral	150	12	300	Monday, February 2, 2015
155	SK	normal	NAD	daily	no	1	sodium valproate	tablet	oral	100	12	400	Friday, July 24, 2020
-	-	-	-	biannual	-	2	clobazam	tablet	oral	5	12	10	Friday, July 24, 2020
156	N	normal	hyperthyroidisn	yearly	no	1	oxcarbazepine	tablet	oral	450	12	900	Wednesday, October 9, 2019
-	-	-	-	daily	-	2	clobazam	tablet	oral	5	12	10	Wednesday, October 9, 2019
157	AS	normal	NAD	weekly	no	1	clobazam	tablet	oral	10	12	20	Sunday, June 10, 2018
-	-	-	-	-	-	2	phenytoin	tablet	oral	50	12	100	Sunday, June 10, 2018
158	NK	normal	NAD	monthly	no	1	carbamazepine	tablet	oral	400	12	800	Saturday, February 7, 2015
-	-	-	-	monthly	-	2	levetiracetam	tablet	oral	500	12	1000	Saturday, February 7, 2015
159	MS	normal	NAD	sporadic	no	1	levetiracetam	tablet	oral	500	12	1000	02.09.2015
-	-	-	-	monthly	-	2	clobazam	tablet	oral	10	12	20	Wednesday, March 2, 2016
-	-	-	-	-	-	3	sodium valproate	tablet	oral	500	12	1000	Tuesday, February 3, 2015
160	NS	normal	NAD	monthly	no	1	levetiracetam	tablet	oral	500	12	1000	Friday, October 9, 2020
-	-	-	-	-	-	2	clobazam	tablet	oral	5	12	10	Saturday, March 9, 2019
-	-	-	-	-	-	3	carbamazepine	tablet	oral	400	12	800	Monday, May 4, 2020
161	HK	normal	hyperthyroidisn	monthly	no	1	clobazam	tablet	oral	10	12	20	Saturday, June 6, 2020
-	-	-	-	-	-	2	topiramate	tablet	oral	25	24	25	Tuesday, July 7, 2020
-	-	-	-	-	-	3	lamotrigine	tablet	oral	200	12	400	Tuesday, March 3, 2020
162	AS	normal	NAD	weekly	no	1	sodium valproate	tablet	oral	500	12	1000	Saturday, August 1, 2015
-	-	-	-	-	-	2	oxcarbazepine	tablet	oral	150	12	300	Saturday, August 1, 2015
-	-	-	-	-	-	3	clobazam	tablet	oral	10	24	10	Saturday, August 1, 2015
163	SK	normal	NAD	monthly	no	1	sodium valproate	syrup	oral	300	12	600	Friday, February 2, 2018
-	-	-	-	-	-	2	lacosamide	tablet	oral	100	12	200	Friday, February 2, 2018
-	-	-	-	-	-	3	levetiracetam	tablet	oral	250	12	500	Friday, March 2, 2018
164	P	normal	NAD	daily	no	1	phenytoin	tablet	oral	50	12	100	Sunday, June 7, 2020
-	-	-	-	weekly	-	2	levetiracetam	tablet	oral	250	12	500	Saturday, July 4, 2020

S.No	Initials	Date till continuation of drug	Dose after modification on the day of enrollment	follow up 3 months	ADR if any	controlled y/n
136	AK	Friday, February 7, 2020	increased to 1200	continued same	no	yes
-	-	Saturday, August 1, 2020	continued same	continued same	no	
137	IK	Tuesday, February 11, 2020	continued same	continued same	no	yes
138	RK	Friday, February 14, 2020	continued same	carbamazepine added 300 mg BD	itching	no
-	-	Friday, February 14, 2020	continued same	continued same	no	
-	-	Monday, July 6, 2020	continued same	continued same	no	
139	P	Saturday, July 25, 2020	continued same	continued same	no	yes
140	BK	Monday, March 2, 2020	continued same	continued same	no	yes
141	HM	Friday, November 6, 2020	increased to 1200	continued same	no	no
142	N	Tuesday, November 24, 2020	continued same	lost to follow up	no	lost to follow up
143	K	Tuesday, December 1, 2020	increased to 1200	continued same	no	yes
-	-	Tuesday, December 1, 2020	continued same	continued same clobazam added 10	no	
144	A	Tuesday, December 1, 2020	increased to 200	continued same	no	lost to follow up
-	-	Tuesday, December 1, 2020	continued same	continued same	no	
145	MK	Tuesday, December 1, 2020	continued same	continued same	no	yes
146	AG	Sunday, December 27, 2020	continued same	continued same	no	yes
-	-	Sunday, December 27, 2020	continued same	increased to 20	no	
147	LK	Friday, December 25, 2020	continued same	increased to 600	no	no
148	SK	Tuesday, October 20, 2020	continued same	continued same	no	yes
149	AS	Friday, September 11, 2020	continued same	increased to 600	no	no
-	-	Friday, September 11, 2020	continued same	continued same	no	
-	-	Friday, September 11, 2020	continued same	continued same	no	
150	BK	Tuesday, September 22, 2020	continued same	continued same	no	yes
151	SS	Friday, October 30, 2020	continued same	continued same	no	no
-	-	Friday, October 30, 2020	continued same	continued same	no	
152	GK	Friday, October 1, 2021	continued same	continued same	no	no
-	-	Friday, October 1, 2021	continued same	increased to 1000	no	
153	SS	Friday, September 4, 2020	continued same	continued same	no	yes
154	HK	Friday, August 14, 2020	continued same	continued same	no	yes
155	SK	Friday, August 14, 2020	continued same	Oxcarbazepine 300 added	no	yes
-	-	Friday, August 14, 2020	continued same	continued same	no	
156	N	Friday, October 9, 2020	continued same	carbamazepine added 200 mg	no	yes
-	-	Friday, October 9, 2020	increased to 20	continued same	no	
157	AS	Friday, July 31, 2020	continued same	continued same	no	no
-	-	Friday, July 31, 2020	continued same	continued same	no	
158	NK	Tuesday, August 18, 2020	continued same	increased to 1200 and clobazam 10 added	no	yes
-	-	Tuesday, August 18, 2020	continued same	continued same	no	
159	MS	Tuesday, August 25, 2020	continued same	1500 mg	no	no
-	-	Tuesday, August 25, 2020	continued same	continued same	no	
-	-	Tuesday, August 25, 2020	continued same	continued same	no	
160	NS	Tuesday, March 2, 2021	continued same	continued same	no	yes
-	-	Friday, October 9, 2020	increased to 20	continued same	no	
-	-	Friday, October 9, 2020	continued same	continued same	no	
161	HK	Tuesday, July 14, 2020	continued same	continued same	no	yes
-	-	Tuesday, July 14, 2020	continued same	continued same	no	
-	-	Tuesday, July 14, 2020	continued same	continued same	no	
162	AS	Tuesday, October 6, 2020	continued same	continued same	no	yes
-	-	Tuesday, October 6, 2020	continued same	continued same	no	
-	-	Tuesday, October 6, 2020	continued same	continued same	no	
163	SK	Tuesday, June 30, 2020	continued same	continued same	no	yes
-	-	Tuesday, June 30, 2020	continued same	continued same	no	
-	-	Tuesday, June 30, 2020	increased to 1000	continued same	no	
164	P	Saturday, July 4, 2020	increased to 200	continued same	no	lost to follow up
-	-	Tuesday, July 7, 2020	increased to 1000	lost to follow up	no	

S.No	Initials	Age(yr)	Age at onset of seizures (years)	gender	residential area	family history	risk factors	semiology	Seizure Cluster if any	Seizures/ day	Duration(seconds)	Seizure in last 24 hr	MRI findings	EEG findings
165	JS	30	10	m	urban	positive	no	GTCS	yes	6	240	3	cerebral atrophy	normal
-	-	-	-	-	-	-	-	GTCS	yes	6	-	-	-	-
166	SK	36	1	f	urban	negative	no	GTCS	no	2	120	no	normal	no record
-	-	-	-	-	-	-	-	GTCS	no	2	-	-	-	-
167	MK	26	-	f	rural	negative	no	GTCS	no	3	120	no	normal	no record
-	-	-	9	-	-	-	-	GTCS	no	3	-	-	-	-
-	-	-	-	-	-	-	-	GTCS	no	3	-	-	-	-
168	S	40	23	f	rural	positive	no	GTCS	no	1	300	no	normal	normal
169	PR	35	15	f	rural	positive	no	GTCS	no	2	600	no	normal	normal
170	M	14	12	m	rural	positive	no	GTCS	no	1	120	no	normal	normal
171	M	16	11	f	rural	negative	no	tonic clonic	no	2	240	no	normal	no record
-	-	-	-	-	-	-	-	tonic clonic	no	2	-	-	-	-
-	-	-	-	-	-	-	-	tonic clonic	no	2	-	-	-	-
172	A	15	2 months	m	rural	negative	no	GTCS	no	3	600	no	normal	no record
-	-	-	-	-	-	-	-	GTCS	no	3	-	-	-	-
-	-	-	-	-	-	-	-	GTCS	no	3	-	-	-	-
173	P	18	10	f	rural	negative	no	GTCS	no	2	60	no	normal	no record
-	-	-	-	-	-	-	-	GTCS	no	2	-	-	-	-
174	RR	42	34	f	rural	positive	no	GTCS	no	1	120	no	normal	normal
175	MK	18	11	f	rural	negative	no	GTCS	no	2	120	no	normal	normal
-	-	-	-	-	-	-	-	GTCS	no	2	-	-	-	-
176	R	14	13	f	rural	negative	no	GTCS	no	1	120	no	normal	no record
177	JB	8	3	m	urban	positive	no	GTCS	yes	5	180	2	normal	no record
-	-	-	-	-	-	-	-	GTCS	yes	5	-	-	-	-
-	-	-	-	-	-	-	-	GTCS	yes	5	-	-	-	-
178	GK	33	21	f	rural	negative	no	GTCS	no	2	240	no	normal	normal
179	MK	19	1	f	rural	negative	no	GTCS	no	2	240	no	normal	no record
180	KS	20	12	m	urban	negative	no	GTCS	no	1	180	no	normal	no record
-	-	-	-	-	-	-	-	GTCS	no	1	-	-	-	-
181	KT	27	15	f	rural	negative	no	GTCS	no	2	240	no	normal	no record
-	-	-	-	-	-	-	-	GTCS	no	2	-	-	-	-
-	-	-	-	-	-	-	-	GTCS	no	2	-	-	-	-
182	RK	24	23	m	urban	negative	no	absence	no	2	120	no	normal	no record
-	-	-	-	-	-	-	-	absence	no	2	-	-	-	-
-	-	-	-	-	-	-	-	absence	no	2	-	-	-	-
183	MS	23	15	m	urban	negative	fever	GTCS	no	2	60	no	normal	no record
184	AS	17	11	m	rural	negative	no	GTCS	no	1	60	no	normal	normal
-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

S.No	Initials	CNS examination	comorbidity	Seizure frequency	seizure video	S.No of drugs used in patients	Generic name at start of medication	dosage form	route	dose (mg)	frequency (hrly)	daily dose (mg)	start date of drug
165	JS	normal	NAD	monthly	no	1	carbamazepine	tablet	oral	400	12	800	Saturday, February 5, 2005
-	-	-	-	-	-	2	levetiracetam	tablet	oral	1000	12	2000	Tuesday, February 3, 2004
166	SK	normal	NAD	monthly	no	1	oxcarbazepine	tablet	oral	300	12	600	Thursday, March 2, 2017
-	-	-	-	-	-	2	levetiracetam	tablet	oral	500	12	1000	Monday, February 4, 2019
167	MK	normal	NAD	monthly	no	1	clobazam	tablet	oral	5	24	5	Monday, March 2, 2020
-	-	-	-	monthly	-	2	levetiracetam	tablet	oral	250	12	500	Monday, March 2, 2020
-	-	-	-	-	-	3	phenytoin	tablet	oral	100	12	200	Sunday, March 4, 2018
168	S	normal	NAD	daily	no	1	phenytoin	tablet	oral	100	12	200	Tuesday, June 4, 2019
169	PR	normal	NAD	sporadic	no	1	levetiracetam	tablet	oral	500	12	1000	Wednesday, April 2, 2014
170	M	normal	NAD	daily	no	1	levetiracetam	tablet	oral	500	12	1000	Wednesday, April 2, 2014
171	M	normal	NAD	monthly	no	1	phenytoin	tablet	oral	100	12	200	Wednesday, March 29, 2017
-	-	-	-	sporadic	-	2	sodium valproate	tablet	oral	250	12	500	Wednesday, March 29, 2017
-	-	-	-	-	-	3	phenobarbitone	tablet	oral	60	12	120	Wednesday, March 29, 2017
172	A	normal	NAD	daily	no	1	phenytoin	tablet	oral	150	12	300	Saturday, October 29, 2016
-	-	-	-	-	-	2	phenobarbitone	tablet	oral	30	12	60	Saturday, October 29, 2016
-	-	-	-	monthly	-	3	clobazam	tablet	oral	10	24	10	Saturday, October 29, 2016
173	P	normal	NAD	monthly	no	1	sodium valproate	tablet	oral	500	12	1000	Monday, June 2, 2014
-	-	-	-	monthly	-	2	carbamazepine	tablet	oral	200	12	400	Monday, June 2, 2014
174	RR	normal	NAD	weekly	no	1	phenytoin	tablet	oral	150	12	300	Sunday, September 1, 2019
175	MK	normal	NAD	weekly	no	1	oxcarbazepine	tablet	oral	900	12	1800	Sunday, August 6, 2017
-	-	-	-	-	-	2	clobazam	tablet	oral	10	12	20	Sunday, August 6, 2017
176	R	normal	NAD	sporadic	no	1	levetiracetam	tablet	oral	500	12	1000	Monday, September 6, 2010
177	JB	normal	NAD	sporadic	no	1	carbamazepine	tablet	oral	300	12	600	Monday, April 5, 2004
-	-	-	-	-	-	2	levetiracetam	tablet	oral	500	12	1000	Monday, April 5, 2004
-	-	-	-	-	-	3	clobazam	tablet	oral	10	24	10	Monday, April 5, 2004
178	GK	normal	NAD	weekly	no	1	sodium valproate	tablet	oral	500	12	1000	Sunday, September 1, 2019
179	MK	normal	NAD	sporadic	no	1	sodium valproate	tablet	oral	400	12	800	Sunday, July 2, 2017
180	KS	normal	NAD	daily	no	1	levetiracetam	tablet	oral	750	12	1500	Wednesday, September 5, 2018
-	-	-	-	-	-	2	clobazam	tablet	oral	10	24	10	Wednesday, September 5, 2018
181	KT	normal	NAD	sporadic	no	1	oxcarbazepine	tablet	oral	300	12	600	Thursday, September 6, 2018
-	-	-	-	-	-	2	phenytoin	tablet	oral	100	24	100	Friday, September 7, 2018
-	-	-	-	-	-	3	sodium valproate	tablet	oral	300	12	600	Saturday, September 8, 2018
182	RK	normal	NAD	sporadic	no	1	oxcarbazepine	tablet	oral	600	12	1200	Sunday, September 9, 2018
-	-	-	-	-	-	2	sodium valproate	tablet	oral	500	12	1000	Sunday, July 2, 2017
-	-	-	-	-	-	3	carbamazepine	tablet	oral	10	24	10	Monday, July 3, 2017
183	MS	normal	NAD	sporadic	no	1	phenytoin	tablet	oral	50	12	100	Wednesday, July 4, 2018
184	AS	normal	NAD	sporadic	no	1	sodium valproate	tablet	oral	500	12	1000	Thursday, March 2, 2017
-	-	-	-	-	-	2	oxcarbazepine	tablet	oral	600	12	1200	Friday, March 3, 2017

S.No	Initials	Date till continuation of drug	Dose after modification on the day of enrollment	follow up 3 months	ADR if any	controlled y/n
165	JS	Sunday, December 20, 2020	increased to 1600	continued same	no	no
-	-	Sunday, December 20, 2020	continued same	continued same	no	
166	SK	Friday, March 20, 2020	continued same	continued same	no	yes
-	-	Friday, March 20, 2020	continued same	continued same	no	
167	MK	Friday, October 23, 2020	continued same	clobazam added 10 mg BD	no	no
-	-	Friday, October 23, 2020	continued same	continued same	no	
-	-	Friday, October 23, 2020	continued same	continued same	no	
168	S	Saturday, July 4, 2020	continued same	continued same	no	lost to follow up
169	PR	Tuesday, October 29, 2019	continued same	clobazam added 10	no	lost to follow up
170	M	Tuesday, October 29, 2019	continued same	continued same	no	lost to follow up
171	M	Tuesday, October 29, 2019	continued same	continued same	no	no
-	-	Tuesday, October 29, 2019	continued same	increased to 1000	no	
-	-	Tuesday, October 29, 2019	continued same	continued same	no	
172	A	Friday, November 29, 2019	increased to 600	continued same	no	no
-	-	Friday, November 29, 2019	increaesd to 120	continued same	no	
-	-	Friday, November 29, 2019	continued same	continued same	no	
173	P	Tuesday, November 19, 2019	continued same	continued same	no	yes
-	-	Tuesday, November 19, 2019	continued same	continued same	no	
174	RR	Monday, September 30, 2019	continued same	lost to follow up	no	lost to follow up
175	MK	Tuesday, October 8, 2019	continued same	lost to follow up	no	lost to follow up
-	-	Tuesday, October 8, 2019	continued same	lost to follow up	no	
176	R	Tuesday, September 24, 2019	continued same	continued same	no	yes
177	JB	Thursday, September 26, 2019	increaesd to 1200	continued same	no	yes
-	-	Thursday, September 26, 2019	continued same	continued same	no	
-	-	Thursday, September 26, 2019	continued same	continued same	no	
178	GK	Thursday, October 31, 2019	continued same	lost to follow up	no	lost to follow up
179	MK	Friday, October 11, 2019	continued same	continued same	no	no
180	KS	Sunday, December 15, 2019	continued same	clobazam added 10	no	no
-	-	Sunday, December 15, 2019	continued same	increased to 20	no	
181	KT	Friday, October 11, 2019	continued same	continued same	no	yes
-	-	Friday, October 11, 2019	continued same	dose increased 450 mg BD	no	
-	-	Friday, October 11, 2019	continued same	continued same	no	
182	RK	Tuesday, October 15, 2019	continued same	continued same	no	yes
-	-	Tuesday, October 15, 2019	continued same	continued same	no	
-	-	Tuesday, October 15, 2019	continued same	continued same	no	
183	MS	Saturday, September 14, 2019	continued same	continued same	no	no
184	AS	Sunday, September 15, 2019	continued same	continued same	no	no
-	-	Monday, September 16, 2019	continued same	continued same	no	

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No. BFUHS/2K23p-TH/ 37 Date 1/1/24

The Principal
Dayanand Medical College & Hospital
Ludhiana

Subject:: Approval of Plan of Thesis.

This is to inform you that the Faculty of Medical Sciences in its meeting held on 25.09.2023 has approved the plan of thesis of **Simrat Kaur**, a student of your college for **MD Pharmacology** along with the names of Supervisor/Co-Supervisor as under:-

Topic Plan of Thesis
To study the incidence of cluster seizures and evaluation of pharmacological management strategies among cohort of patients with epilepsy .

Supervisor	Co-Supervisor:-	Co-Supervisor:-
Dr. Sandeep Kaushal	Dr. Gagandeep Singh	Dr. Kanchan Gupta
Prof. & Head	Prof. & Head	Professor
Dept. of Pharmacology	Dept. of Neurology	Dept. of Pharmacology

The student may submit the thesis in triplicate alongwith the plan in triplicate also, to the Controller of Examinations, BFUHS, Faridkot, at least six months before the commencement of theory examination, if he/she is otherwise eligible to take the examination. He /She may be directed to attach a photocopy of this letter with the forwarding letter while submitting thesis in the University along with the letter of approval of University for change of supervisor/Co-Supervisor, change of topic, if any.

Controller of Examinations

Note :

1. *If any discrepancy found regarding topic of thesis or Supervisor/Co-Supervisor, inform undersigned within one month after issue of this letter.*

TO STUDY THE INCIDENCE OF CLUSTER SEIZURES AND EVALUATION OF PHARMACOLOGICAL MANAGEMENT STRATEGIES AMONG COHORT OF PATIENTS WITH EPILEPSY

THESIS PROPOSAL

FOR APPROVAL OF SUBJECT OF THESIS TO BE SUBMITTED IN

PARTIAL FULFILMENT OF THE REQUIREMENTS

FOR THE DEGREE OF

MD

In

PHARMACOLOGY

OF THE

BABA FARID UNIVERSITY OF HEALTH SCIENCES

FARIDKOT

AUGUST, 2022 **DR. SIMRAT KAUR**

DEPARTMENT OF PHARMACOLOGY
DAYANAND MEDICAL COLLEGE AND HOSPITAL
LUDHIANA

ABSTRACT OF PLAN OF THESIS

Title	To study the Incidence of cluster seizures and evaluation of pharmacological management strategies among cohort of patients with epilepsy
For the degree of	MD Pharmacology
Name of the candidate	Dr. Simrat Kaur
Supervisor	Dr. Sandeep Kaushal, Professor & Head, Department of Pharmacology, DMCH, Ludhiana.
Co-supervisor	Dr. Gagandeep Singh, Professor & Head, Department of Neurology, DMCH, Ludhiana Dr. Kanchan Gupta, Professor, Department of Pharmacology, DMCH, Ludhiana.
Institution	Dayanand Medical College & Hospital, Ludhiana
University	Baba Farid University of Health Sciences, Faridkot

Introduction: There is an estimated frequency of cluster seizures in the range of 3%-76% worldwide among patients of epilepsy. High frequency in the first 12 months after onset of epilepsy are associated with cluster seizures.

Aims & Objectives: 1. To study the Incidence of cluster seizures among cohort of patients with epilepsy.

2. Evaluation of pharmacological management strategies in patients with epilepsy.

Material & Methods: This study will be conducted in the new onset cluster seizure patients with epilepsy, attending neurology OPD and epilepsy clinic. Patients will be started on monotherapy of AEDs and after the stable dose of monotherapy follow up will be done for 3 months minimum. Patients with non epileptic seizures will be excluded. The data from each patient will be entered on a preformed Proforma.

Clinical Significance: This study will help to assess the incidence of cluster seizures in epileptic patients

Keywords: Epilepsy, Cluster seizures, AEDs, Seizure diary.

(Signature)	(Signature)	(Signature)	(Signature)	(Signature)
Candidate	Co-supervisor	Co- supervisor	Supervisor	Principal

CERTIFICATE OF FACILITIES AVAILABLE

This is to certify that the facilities for work on the subject of thesis entitled "**TO STUDY THE INCIDENCE OF CLUSTER SEIZURES AND EVALUATION OF PHARMACOLOGICAL MANAGEMENT STRATEGIES AMONG COHORT OF PATIENTS WITH EPILEPSY**" exist in the Department of Pharmacology, Dayanand Medical College & Hospital, Ludhiana and will be provided to the candidate. We will see that the data being included in the thesis are genuine and is collected by the candidate herself under our supervision and guidance.

Supervisors

Dr. Sandeep Kaushal
Professor & Head
Department of Pharmacology
DMCH, Ludhiana

Co-Supervisor

Dr. Gagandeep Singh
Professor & Head
Department of Neurology
DMCH, Ludhiana

Dr. Kanchan Gupta
Professor
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Head of the Department

Dr. Sandeep Kaushal
Professor & Head
Department of Pharmacology
DMCH, Ludhiana

Place: LUDHIANA

Date: 7/9/22

APPROVAL PROFORMA
BY RESEARCH & ETHICAL COMMITTEE
DAYANAND MEDICAL COLLEGE & HOSPITAL, LUDHIANA

Name of candidate	Dr. Simrat Kaur
Department	Pharmacology
Topic of Thesis	To study the Incidence of cluster seizures and evaluation of pharmacological management strategies among cohort of patients with epilepsy
Likely date of appearing in PG examination	May/June, 2024
Date of enrolment	2-May-2022
Name of Head of Department	Dr. Sandeep Kaushal
1) Supervisor **2) Co-Supervisor**	Dr. Sandeep Kaushal Dr. Gagandeep Singh Dr. Kanchan Gupta
Signature of Members of Research Committee with Stamp	**Signature of Members of Ethics Committee with Stamp**
Dr. Harpreet Kaur (Professor & Head, Pathology)	Mr. R K Sharma (Legal Expert)
Dr. Jaspal Singh (Professor & Head, Surgery)	Dr. Ramit Mahajan (Associate Professor, Gastroenterology)
Dr. Dinesh Gupta (Professor & Head, Medicine)	Dr. Anu Sharma (Professor, Anatomy)
Dr. Sandeep Kaushal (Dean Academics & Professor & Head, Pharmacology)	Dr. Sandeep Kaushal (Dean Academics & Professor & Head, Pharmacology)
Dr. Gurpreet S Wander (Vice Principal)	Dr. Gurpreet S Wander (Vice Principal & Professor & Head, Cardiology)
	Dr. Gagandeep Singh (Secretary, Ethics Committee Professor & Head, Neurology)

Approved: Yes / ~~No~~

Dr. Sandeep Puri
Chairperson
Research Committee

Chairperson
Research Committee

Approved: Yes / ~~No~~

Prof. Arvind Malhotra
Chairman
Ethics Committee

Chairperson
Ethics Committee

BABA FARID UNIVERSITY OF HEALTH SCIENCES, FARIDKOT

PROFORMA FOR REGISTRATION OF SUBJECT FOR DISSERTATION

1	NAME OF THE CANDIDATE AND ADDRESS	Dr. Simrat Kaur H.No. 1417 New Civil lines Dutt road, Moga, Punjab Pin-142001
2	NAME OF THE INSTITUTE	DAYANAND MEDICAL COLLEGE AND HOSPITAL, LUDHIANA
3	COURSE OF STUDY AND SUBJECT	MD Pharmacology
4	DATE OF ADMISSION OF COURSE	02-05-2022
5	TITLE OF THE TOPIC	TO STUDY THE INCIDENCE OF CLUSTER SEIZURES AND EVALUATION OF PHARMACOLOGICAL MANAGEMENT STRATEGIES AMONG COHORT OF PATIENTS WITH EPILEPSY

6. BRIEF RESUME OF THE INTENDED WORK

6.1 NEED FOR THE STUDY

Epilepsy is one of the most frequent and disabling neurologic conditions, yet we have an incomplete understanding of the detailed pathophysiology and thus, treatment rationale for much of epilepsy.[1] Our understanding is improving with more analysis along with identification of novel drug targets for effective management of epilepsy. Epilepsy is particularly applicable to address the issue of clustering, as it appears that for some individuals (clusters), the probability of a seizure is greater in the setting of recent seizures.[2] The frequency of seizure clusters has been reported in the range of 3% - 76% worldwide among patients with epilepsy.[3] Such high variability in the prevalence can be attributed to the lack of proper definition.[4]

Prevalence of seizure clusters varies significantly in different studies depending on the definitions used. In another story by Et al Forty-three percent of patients who were keeping a seizure diary met the clinical definition of 3 or more seizures in 24 hrs.[5] The wide range in estimation of frequency are due to the lack of a precise definition for seizure clusters, difference in the type of study, difference in the population studied and different methodology for collecting information.[3] A very similar phenomenon to Seizure clusters called the “rebound effect” is exhibited by an increased occurrence of epileptic seizures which follows an abrupt withdrawal of Antiseizure Medications.[6]

Seizure clusters, also called acute repetitive seizure (ARS), are generally referred to seizures that occurs frequently in patients with epilepsy.[3] Refractory Status Epilepticus (RSE) is most often symptomatic of an acute neurologic condition or neuro-degenerative disease. Treatment for RSE is difficult, usually requiring intensive support of vital functions.[7] These repetitive seizures are not uncommon and place a burden on patients and their caretakers. These tightly grouped seizures represent an alarming clinical condition, and if not treated vigorously and efficiently, may lead to status epilepticus

(SE), a life-threatening condition.[8] Multifocal epilepsy , generalized epilepsy, remote history of CNS infection, and focal cortical dysplasia are also identified as risk for seizure clusters. Seizure clusters can give rise to increased emergency room visits or hospitalization. They have negative impact on productivity, disrupting daily life, studies, and work of the patients.[4] Though the negative impact of epilepsy on patient well-being and Quality of life is well known, less is known about the impact of Seizure clusters.[9] History of seizure clusters and status epilepticus , head trauma , earlier age of seizure onset and high seizure frequency in the first 12 months after the onset of epilepsy (one weekly seizure or more) are associated with seizure clusters.[10]

We have planned this study to evaluate incidence of seizure clusters in our cohort of patients and look at effectiveness and sequelae of various pharmacological treatment modalities employed longitudinally over period of time. The study includes retrospective cases of 3 years duration and prospective study of 1 year in cohort of patient with epilepsy.

6.2 REVIEW OF LITERATURE

A “seizure” is a paroxysmal alteration of neurologic function caused by synchronous discharge of neurons in the brain. “Epilepsy” is the condition of recurrent, unprovoked seizures. Epilepsy has numerous causes, each reflecting underlying brain dysfunction.[2] Seizure presentation depends on location of onset in the brain, patterns of propagation, maturity of the brain, confounding disease processes, sleep–wake cycle, medications, and a variety of other factors. Seizures can affect sensory, motor, and autonomic function; emotional state; memory; cognition; or behaviour.[11] Epilepsy classification is the key tool in evaluating an individual presenting with seizures.[12]

The International league against Epilepsy (ILAE) has classified epilepsy as.[13]

(A) Focal seizures

1. Motor
   -Tonic
   -Atonic
   -Myoclonic
   -Epileptic spasms
   -Clonic
   -Hyper motor
2. Non motor
   -Sensory
   -Emotional
   -Autonomic
   -Cognitive

(B) Generalized

1. Motor
   -Tonic clonic
   -Myoclonic
   -Tonic
   -Atonic
   - Clonic

-Epileptic spasms

2.Absence

-Typical

-Atypical

-Myoclonic

(C) Unknown onset

1.Motor

-Tonic clonic

-Atonic

-Epileptic spasms

2.Non motor

(D) unclassified

Seizure cluster is not listed in the International League Against Epilepsy (ILAE) Commission on Classification and Terminology. There is no universally accepted definition for a cluster of seizures in patients with epilepsy. A broad definition of seizure clusters is acute episodes of deterioration in seizure control. It could be defined as a series of grouped seizures that have short interictal periods.[14] It has also been hypothesized that seizure clusters may represent a “self-triggering” mechanism and that shorter seizures are less likely than longer seizures to sufficiently activate seizure-termination mechanisms. Seizure clusters are typically defined by the number of seizures over a specific interval or as an increased seizure frequency above baseline recognizable by patient or family.[15] Clinical definitions include: two or more seizures in six hours, two or more seizures in 24 hrs, two to four seizures in less than 48 h, and two generalized tonic clonic or three complex partial seizures in 4h. Saba et al has defined cluster seizure as “An episode of multiple complex partial or generalized (tonic, clonic , tonic clonic, atypical absence, or myoclonic) seizures occurring within a 24-h period in adults or a 12-h period in children, with a pattern distinguishable from the patient’s usual seizure pattern, and with onset readily recognizable by patients or guardian.[16] Potential risk factors include failure of seizure-terminating mechanisms and increased focal

neuronal excitability. For many patients, seizure clusters impair quality of life and increase morbidity due to hospitalization, status epilepticus, postictal psychosis and at times mortality.

Seizure clusters were associated with earlier age of seizure onset, symptomatic generalized epilepsy (SGE), central nervous system (CNS) infection, cortical dysplasia, status epilepticus.[17] Many researchers have paid attention to the potential factors contributing to Seizure Clusters and they also estimated the patient's risk of Seizure Clusters. Factors associated with Seizure Clusters in PWE include previous head trauma, extratemporal seizure localization, history of status epilepticus, higher frequency of seizures, intractable epilepsy, symptomatic generalized epilepsy, focal epilepsy (vs. idiopathic generalized epilepsy), epilepsy onset at early age, and longer duration of epilepsy.[18]

The unpredictable nature of seizures and seizure clusters, adequate treatment of seizure clusters involves 3 phases: developing and becoming familiar with an action plan to be implemented in the event of a seizure; ensuring necessary medications are obtained and are carried with the patient and/or are accessible at all locations frequented by the patient; and implementing the action plan on first signs of a seizure cluster (which may simply be first signs of a seizure in some patients).[19] The treatment of seizure clusters must be individualized. It must depend on the type, frequency, severity, and duration of seizures in a cluster, and whether episodes have been known to progress to prolonged seizures or status epilepticus.[6] Use of benzodiazepine rescue medications is the cornerstone in acute management of seizure clusters that can help to end clusters and reduce emergency room visits. However, studies have shown that benzodiazepines are largely underutilized in patients with seizure clusters.[17] Common seizure cluster treatments for mild seizure clusters include extra doses of the usual antiseizure medications. In addition benzodiazepines can be used (oral clobazam or sublingual benzodiazepines) in particular diazepam, and lorazepam.[6] Orally disintegrated clonazepam and oral clobazam have also been used in Seizure Clusters; Midazolam can be

successfully administered intramuscularly and via inhalational route also. Intramuscular midazolam had superior effectiveness in stopping convulsive status epilepticus compared with intravenous lorazepam when administered via an autoinjector by paramedics prior to hospital arrival.[20]

There is a lot of variation in data across the world regarding seizure clusters, treatment options, still there is no clear conclusion on to the prevalence, treatment options and effectiveness of various therapies in patients with seizure clusters.

6.3 AIMS AND OBJECTIVES OF THE STUDY

1. To study the Incidence of cluster seizures among cohort of patients with epilepsy.
2. Evaluation of pharmacological management strategies in patients with epilepsy.

7. MATERIALS AND METHODS

7.1 SOURCE OF DATA

This study will be conducted in patients with epilepsy at Dayanand Medical Hospital in Ludhiana city.

7.2 METHODS OF COLLECTION OF DATA

Consenting patients / assenting children and their parents attending Neurology/Epilepsy clinic who fulfill all the inclusion criteria and none of the exclusion criteria will be included in the study.

INCLUSION CRITERIA

1) Age: Any
2) Gender: either
3) Known case of epilepsy on Anti-epileptic drugs
4) Subjects reporting >3 seizures in 24 hours
5) Co-morbid conditions: Any

EXCLUSION CRITERIA

1) Non epileptic seizures
2) Non consenting patients

STUDY DESIGN

This is a three year retrospective study and one year prospective study in which patients having seizure clusters (who are initiated on treatment or being treated with AEDs) will be enrolled. Patient demographics i.e. Gender, age, height, weight, basal metabolic index and socioeconomic status (using modified Kuppuswamy scale) along with clinical characteristics such as history of past and present seizures, clusters; AEDs treatment and other concomitant treatment will be recorded. Patients will be started on monotherapy of AEDs and after the stable dose of monotherapy follow up will be done for 3 months minimum. The relevant baseline investigations include EEG/neuroimaging (as applicable) will be recorded. The seizure frequency will be recorded using seizure diary.

DURATION OF STUDY

Total duration 4 Years (3 year retrospective and 1 year prospective study)

15th September 2019 - 14th September 2022(Retrospective date)

15th September 2022 - 14th September 2023(Prospective date)

OUTCOME PARAMETERS

Assessment of incidence of cluster seizures among cohort of patients with epilepsy.

Assessment of efficacy, safety and tolerability of pharmacological options used for management of cluster seizures based on seizure semiology, frequency and control of seizures.

STATISTICAL ANALYSIS

The obtained results will be entered in Microsoft excel and analysed using descriptive statistics. Data will be described in terms of range, mean ± SD, median, frequencies (number of cases) and relative frequencies (percentage) as appropriate. All statistical calculations will be done using (Statistical package for the Social Science) SPSS 21 version (SPSS Inc., Chicago, IL, USA) statistical program for Microsoft Windows.

7.3 DOES THE STUDY REQUIRE ANY INVESTIGATIONS TO BE CONDUCTED ON PATIENTS OR OTHER HUMANS OR ANIMALS? IF SO, PLEASE DESCRIBE BRIEFLY.

Yes, to evaluate the seizure aetiology and predict safety and tolerability.

7.4 ETHICAL CLEARANCE BEING OBTAINED FROM YOUR INSTITUTION IN CASE OF 7.3?

Ethical clearance attached along with

8. LIST OF REFERENCES

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PROFORMA

Date _____ Sr No._____

MRD NO._____ Name_____ Age/Sex _____/_____

Father's name/husband's name_____ Address_____

Head of the family_____ Occupation of head of family _____

Education of head of family _____ Family income _____

Rural/urban _____ Phone no_____ Occupation_____

Socio economic status_____ Age at onset of seizures _____

Seizure semiology_____ Seizure type_____ Seizure frequency_____

Past history of seizure _____ Seizure cluster if any _____

No. of seizures/day_____ Last seizure _____ Date and time of last AED dose_____ No. of seizure episodes in last 24 hrs _____

Duration of each seizure _____Comorbid condition_____ family H/O epilepsy_____

Cluster seizure video recorded: Yes /No If Yes keep copy of video file after consent for video.

Incidence=No. of patients with cluster seizures/total patients with epilepsy

General physical examination

Height(m) _____weight(kg) _____

Systemic examination

CNS: _____

Neuroimaging: EEG_____ MRI_____

FINAL DIAGNOSIS: _____

Treatment history

S. No	Dosage form	Generic name of drug	Dose	Route of drug administration	Frequency	Start date	Stop date	ADR if any

Cluster seizure controlled: yes /no

Signature of candidate **Signature of supervisor**

Modified Kuppuswamy scale

Occupation of the Head of the family

S. No.	Occupation of the Head	Score
1	Legislators, Senior Officials & Managers	10
2	Professionals	9
3	Technicians and Associate Professionals	8
4	Clerks	7
5	Skilled Workers and Shop & Market Sales Workers	6
6	Skilled Agricultural & Fishery Workers	5
7	Craft & Related Trade Workers	4
8	Plant & Machine Operators and Assemblers	3
9	Elementary Occupation	2
10	Unemployed	1

Education of the Head of the family

S. No.	Education of the Head	Score
1	Profession or Honours	7
2	Graduate	6
3	Intermediate or diploma	5
4	High school certificate	4
5	Middle school certificate	3
6	Primary school certificate	2
7	Illiterate	1

Family income

S. No.	Updated Monthly Family Income in Rupees (2012)	Updated Monthly Family Income in Rupees (2018)	Updated Monthly Family Income in Rupees (2020)	Updated Monthly Family Income in Rupees (2021)	Score
2	15,188–30,374	63,182–126,359	99,931–199,861	61,663-123,321	10
3	11,362–15,187	47,266–63,181	74,755 –99,930	46129-61,662	6
4	7594–11,361	31,591–47,265	49,962–74,755	30,831-46,128	4
5	4556–7593	18,953–31,590	29,973– 49,961	18,497-30,830	3
6	1521–4555	6327–18,952	10,002–29,972	6,175-18,496	2
7	≤ 1520	≤ 6326	≤ 10,001	≤ 6174	1

Kuppuswamy socio-economic status scale 2021

S. No.	Score	Socioeconomic Class
1	26–29	Upper (I)
2	16–25	Upper Middle (II)
3	11–15	Lower Middle (III)
4	5–10	Upper Lower (IV)
5	< 5	Lower (V)

Seizure diary

Date	Jan	Feb	Mar	Apr	May	June	July	Aug	Sep	Oct	Nov	Dec
1												
2												
3												
4												
5												
6												
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WHO-UMC CAUSALITY ASSESSMENT SCALE

Causality term	Assessment criteria*
Certain	• Event or laboratory test abnormality, with plausible time relationship to drug intake • Cannot be explained by disease or other drugs • Response to withdrawal plausible (pharmacologically, pathologically) • Event definitive pharmacologically or phenomenologically (i.e. an objective and specific medical disorder or a recognised pharmacological phenomenon) • Rechallenge satisfactory, if necessary
Probable/ Likely	• Event or laboratory test abnormality, with reasonable time relationship to drug intake • Unlikely to be attributed to disease or other drugs • Response to withdrawal clinically reasonable • Rechallenge not required
Possible	• Event or laboratory test abnormality, with reasonable time relationship to drug intake • Could also be explained by disease or other drugs • Information on drug withdrawal may be lacking or unclear
Unlikely	• Event or laboratory test abnormality, with a time to drug intake that makes a relationship improbable (but not impossible) • Disease or other drugs provide plausible explanations
Conditional/ Unclassified	• Event or laboratory test abnormality • More data for proper assessment needed, or • Additional data under examination
Unassessable/ Unclassifiable	• Report suggesting an adverse reaction • Cannot be judged because information is insufficient or contradictory • Data cannot be supplemented or verified

INFORMED PATIENT CONSENT

Date: _____

I…….D/o, W/o, S/o……..…… am willing to participate in the study **"TO STUDY THE INCIDENCE OF CLUSTER SEIZURES AND EVALUATION OF PHARMACOLOGICAL MANAGEMENT STRATEGIES AMONG COHORT OF PATIENTS WITH EPILEPSY"** The procedure with its complications has been explained to me in local vernacular language. I have fully understood that no special tests and extra expenditure in any form, merely for the purpose of thesis is being carried out. I am free to opt out the study any time without assigning any reason.

……. ……
Signature of the Witness Signature of the patient

Name:

Signature of Candidate **Signature of Supervisor**

मरीज अनुमति फार्म

तिथि _____

मैं _____ पत्नी/पुत्र/पुत्री _____

निवासी _____

इस शोधकार्य **"TO STUDY THE INCIDENCE OF CLUSTER SEIZURES AND EVALUATION OF PHARMACOLOGICAL MANAGEMENT STRATEGIES AMONG COHORT OF PATIENTS WITH EPILEPSY"** में भाग लेने के लिए सहमत हूँ। मैं इस शोधकार्य में भाग लेने के लिए अपनी स्वेच्छा से तैयार हूँ। मैं पुष्टि करता/करती हूँ की यह स्वीकृति देने के लिए मुझे कोई आर्थिक प्रलोभन नहीं दिया गया और न ही दबाव डाला गया है। मुझे इस शोधकार्य का उद्देश्य स्पष्ट कर दिया गया है और मुझे यह विश्वास है की यह विज्ञान और मानवता के लाभ के लिए है। मुझे इस शोधकार्य में होने वाले जोखिम के बारे में समझा दिया गया है और मेरी समझ में यह जोखिम बहुत मामुली है।

मैं इस शोधकार्य में भाग लेने के सम्बन्ध में किसी भी समय अपनी अस्वीकृति व्यक्त कर सकता/सकती हूँ और मेरे अस्वीकृति व्यक्त करने का मेरे इलाज पर कोई प्रभाव नहीं पड़ेगा।

_____ _____

गवाह के हस्ताक्षर रोगी के हस्ताक्षर/अंगूठे का निशान

नाम: नाम:

_____

अन्वेषक के हस्ताक्षर

_____

विद्यार्थी के हस्ताक्षर

ਮਰੀਜ਼ ਰਜ਼ਾਮੰਦੀ ਫਾਰਮ

ਮਿਤੀ_____

ਮੈ_____ਪਤਨੀ/ਪੁੱਤਰ/ਪੁੱਤਰੀ_____

ਵਾਸੀ _____

“TO STUDY THE INCIDENCE OF CLUSTER SEIZURES AND EVALUATION OF PHARMACOLOGICAL MANAGEMENT STRATEGIES AMONG COHORT OF PATIENTS WITH EPILEPSY” ਤੇ ਚਲ ਰਹੀ ਖੋਜ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਲਈ ਰਜ਼ਾਮੰਦ ਹਾਂ। ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਲਈ ਮੈ ਆਪਣੀ ਮਰਜ਼ੀ ਨਾਲ ਤਿਆਰ ਹਾਂ। ਮੈ ਇਹ ਦਸਣਾ ਚਾਹੁੰਦਾ ਹਾਂ/ ਚਾਹੁੰਦੀ ਹਾਂ ਕੇ ਇਹ ਰਜ਼ਾਮੰਦੀ ਦੇਣ ਵਾਸਤੇ ਮੈਨੂ ਕਿਸੇ ਵੀ ਤਰਾਂ ਦਾ ਲੋਭ-ਲਾਲਚ ਨਹੀ ਦਿੱਤਾ ਗਿਆ ਅਤੇ ਨਾ ਹੀ ਕੋਈ ਦਬਾ ਪਾਇਆ ਗਿਆ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਦਾ ਮਨੋਰਥ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ ਅਤੇ ਮੈਨੂ ਇਹ ਭਰੋਸਾ ਦਵਾਇਆ ਗਿਆ ਹੈ ਕੇ ਇਹ ਖੋਜ ਵਿਗਿਆਨ ਅਤੇ ਮਾਨਵਤਾ ਦੀ ਭਲਾਈ ਲਈ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਵਿਚ ਹੋਣ ਵਾਲੇ ਖਤਰੇ ਬਾਰੇ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ ਅਤੇ ਮੈਨੂ ਇਹ ਯਕੀਨ ਹੈ ਕੇ ਇਹ ਖਤਰਾ ਬਹੁਤ ਮਾਮੂਲੀ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਦਾ ਢੰਗ – ਤਰੀਕਾ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ।

ਮੈ ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਬਾਰੇ ਆਪਣੀ ਰਜ਼ਾਮੰਦੀ ਕਿਸੇ ਵੀ ਸਮੇ ਵਾਪਸ ਲੈ ਸਕਦਾ ਹਾਂ/ ਸਕਦੀ ਹਾਂ ਅਤੇ ਮੇਰੀ ਰਜ਼ਾਮੰਦੀ ਵਾਪਸ ਲੈਣ ਦਾ ਮੇਰੇ ਇਲਾਜ ਤੇ ਕੋਈ ਅਸਰ ਨਹੀ ਹੋਵੇਗਾ।

_____ _____

ਗਵਾਹ ਦੇ ਹਸਤਾਖਰ ਮਰੀਜ਼ ਦੇ ਹਸਤਾਖਰ

ਮਿਤੀ_____ ਮਿਤੀ_____

ਪਤਾ _____ ਪਤਾ _____

_____

ਨਿਰੀਖਕ ਦੇ ਹਸਤਾਖਰ

_____

ਸਿਖਿਆਰਥੀ ਦੇ ਹਸਤਾਖਰ

Written Assent form

(13 years – 18 years of age)

I _____ son/ daughter of _____ R/o_____ hereby agree to participate in the study entitled "**TO STUDY THE INCIDENCE OF CLUSTER SEIZURES AND EVALUATION OF PHARMACOLOGICAL MANAGEMENT STRATEGIES AMONG COHORT OF PATIENTS WITH EPILEPSY**". I will share the information regarding seizures and their control as and when asked.

Date: Name:

Address: _____

<u>मरीज अनुमति फार्म</u>

<u>(13 वर्ष - 18 वर्ष की आयु)</u>

तिथि _____

मैं _____ पुत्र/पुत्री _____ निवासी _____ इस शोधकार्य **"TO STUDY THE INCIDENCE OF CLUSTER SEIZURES AND EVALUATION OF PHARMACOLOGICAL MANAGEMENT STRATEGIES AMONG COHORT OF PATIENTS WITH EPILEPSY"** में भाग लेने के लिए सहमत हूँ। मैं इस शोधकार्य में भाग लेने के लिए अपनी स्वेच्छा से तैयार हूँ। मैं पुष्टि करता/करती हूँ की यह स्वीकृति देने के लिए मुझे कोई आर्थिक प्रलोभन नहीं दिया गया और न ही दबाव डाला गया है। मुझे इस शोधकार्य का उद्देश्य स्पष्ट कर दिया गया है और मुझे यह विश्वास है की यह विज्ञान और मानवता के लाभ के लिए है। मुझे इस शोधकार्य में होने वाले जोखिम के बारे में समझा दिया गया है और मेरी समझ में यह जोखिम बहुत मामुली है।

मैं इस शोधकार्य में भाग लेने के सम्बन्ध में किसी भी समय अपनी अस्वीकृति व्यक्त कर सकता/सकती हूँ और मेरे अस्वीकृति व्यक्त करने का मेरे इलाज पर कोई प्रभाव नहीं पड़ेगा।

_____ _____

गवाह के हस्ताक्षर रोगी के हस्ताक्षर/अंगूठे का निशान

नाम: नाम:

_____

अन्वेषक के हस्ताक्षर

_____

विद्यार्थी के हस्ताक्षर

ਮਰੀਜ਼ ਰਜ਼ਾਮੰਦੀ ਫਾਰਮ

(13 ਸਾਲ - 18 ਸਾਲ ਦੀ ਉਮਰ)

ਮਿਤੀ_____

ਮੈ_____ ਪੁੱਤਰ/ਪੁੱਤਰੀ_____

ਵਾਸੀ _____ **"TO STUDY THE INCIDENCE OF CLUSTER SEIZURES AND EVALUATION OF PHARMACOLOGICAL MANAGEMENT STRATEGIES AMONG COHORT OF PATIENTS WITH EPILEPSY"** ਤੇ ਚਲ ਰਹੀ ਖੋਜ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਲਈ ਰਜ਼ਾਮੰਦ ਹਾਂ। ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਲਈ ਮੈ ਆਪਣੀ ਮਰਜ਼ੀ ਨਾਲ ਤਿਆਰ ਹਾਂ। ਮੈ ਇਹ ਦਸਣਾ ਚਾਹੁੰਦਾ ਹਾਂ/ ਚਾਹੁੰਦੀ ਹਾਂ ਕੇ ਇਹ ਰਜ਼ਾਮੰਦੀ ਦੇਣ ਵਾਸਤੇ ਮੈਨੂ ਕਿਸੇ ਵੀ ਤਰਾਂ ਦਾ ਲੋਭ-ਲਾਲਚ ਨਹੀ ਦਿੱਤਾ ਗਿਆ ਅਤੇ ਨਾ ਹੀ ਕੋਈ ਦਬਾ ਪਾਇਆ ਗਿਆ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਦਾ ਮਨੋਰਥ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ ਅਤੇ ਮੈਨੂ ਇਹ ਭਰੋਸਾ ਦਵਾਇਆ ਗਿਆ ਹੈ ਕੇ ਇਹ ਖੋਜ ਵਿਗਿਆਨ ਅਤੇ ਮਾਨਵਤਾ ਦੀ ਭਲਾਈ ਲਈ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਵਿਚ ਹੋਣ ਵਾਲੇ ਖਤਰੇ ਬਾਰੇ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ ਅਤੇ ਮੈਨੂ ਇਹ ਯਕੀਨ ਹੈ ਕੇ ਇਹ ਖਤਰਾ ਬਹੁਤ ਮਾਮੂਲੀ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਦਾ ਢੰਗ – ਤਰੀਕਾ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ।

ਮੈ ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਬਾਰੇ ਆਪਣੀ ਰਜ਼ਾਮੰਦੀ ਕਿਸੇ ਵੀ ਸਮੇ ਵਾਪਸ ਲੈ ਸਕਦਾ ਹਾਂ/ ਸਕਦੀ ਹਾਂ ਅਤੇ ਮੇਰੀ ਰਜ਼ਾਮੰਦੀ ਵਾਪਸ ਲੈਣ ਦਾ ਮੇਰੇ ਇਲਾਜ ਤੇ ਕੋਈ ਅਸਰ ਨਹੀ ਹੋਵੇਗਾ।

_____ _____

ਗਵਾਹ ਦੇ ਹਸਤਾਖਰ ਮਰੀਜ਼ ਦੇ ਹਸਤਾਖਰ

ਮਿਤੀ_____ ਮਿਤੀ_____

ਪਤਾ _____ ਪਤਾ _____

_____

ਨਿਰੀਖਕ ਦੇ ਹਸਤਾਖਰ

_____

ਸਿਖਿਆਰਥੀ ਦੇ ਹਸਤਾਖਰ